# A Guide to a "Proper" Diet with "Appropriate" Supplements

[Based on addressing normal and abnormal cell metabolism]

<sup>By</sup> Neil B. Feldman

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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 from "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.

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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 plus "appropriate" supplements for stage IV renal carcinoma patients (like myself), although it also applies to all other cancer patients. My approach is based on evaluating all dietary considerations in light of normal and abnormal cell metabolism. My research is very much a "work-in-progress" and thus subject to change. Some of it is based on information found in these books and resources (the rest is based on credible peer-reviewed articles and papers found in PubMed and similar on-line sources):

1. "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.

2. "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.

3. "**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

4. "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").

5. "**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.

6. "**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.

7. "**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 it 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."<sup>1</sup>

8. "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."<sup>2</sup>

9. "**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.

10. "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.

11. "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

<sup>&</sup>lt;sup>1</sup>From the back cover of the book.

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<sup>&</sup>lt;sup>4</sup>Credit for the concept of five internal "biochemical terrains" goes to Dr. Keith I. Block.

already suffered 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.

12. "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.

13. "**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.

14. **"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."

15. "**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.

16. "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.

17. "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 patients. The book goes into detail about both mainstream and "integrative" cancer treatments with emphasis on the value of proper diet and certain nutritional supplements. Recently, as a result of new research and medical discoveries I have come to question some of their dietary recommendations.

<sup>&</sup>lt;sup>3</sup> From page 10 of the book.

18. "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 went on to pitch several one-sided arguments for adopting a purely vegan diet to prevent or fight cancer. However, after of months of indepth research (and personal experimentation), I could not advocate this approach. There is no clear scientific evidence that plant protein is somehow inherently "healthier" than animal protein for cancer sufferers. All the research and various articles cited in this book appear to be significantly 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 this book. Regardless, this video adds nothing more significant to their overall argument.

19. "**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 going vegan). It is primarily **inflammation** that is likely at the crux of arteriolosclerosis and other cardiovascular diseases. His diet certainly does help reduce inflammation. Meanwhile, the results he achieved were purely anecdotal. They have not been repeated in any random controlled clinical trials (RCTs).

Most of these books share at least three things in common: 1) they were written or coauthored 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".

To sum up, I have read all of these books and researched countless other articles and scholarly papers. Note, however, that I have not meticulously footnoted each of these various sources in the following guide.

I should also note that I am a firm follower of **SBM** (science-based medicine) and **EBM** (evidence-based medicine). All these various books and research articles suggest the essential need for any cancer sufferer to: 1) change to a "proper" diet; 2) add additional "appropriate" supplements to that diet if necessary; and 3) follow their oncologist's recommended drug or radiation therapies.

#### II. COMBATING MISLEADING OR NON-EXISTENT NUTRITIONAL ADVICE

There are still 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", actually true?

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

Other oncologists may plead ignorance on the subject of proper nutrition and diet. They may claim that they were not "sufficiently trained" in the field of nutrition or that the taking of additional supplements may interfere with targeted or chemo therapies. These responses can create a confusing state of affairs for patients. They are then 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 "proper" diet and to take "appropriate" supplements to help fight or prevent cancer. It also outlines what I personally have been doing that has minimized or prevented any serious side effects while I have been taking the targeted anti-angiogenesis TKI drug **Sutent**<sup>®</sup> (**Sunitinib**) and the monoclonal antibody bone agent **Xgeva**<sup>®</sup> (**Denosumab**).

I need to offer one word of caution. Be prepared to discover several nutritional "myths" being challenged or completely busted as you go through this document. That is both the beauty and challenge of good scientific research. It is does not play favorites. We understand far more today than 40 or 50 years ago - which is when much of the flawed and incorrect nutritional advice unfortunately still being dished out was first suggested.

#### III. SOME IMPORTANT CAVEATS

Before discussing the rationale behind the diet and supplements there are several important caveats to consider:

- 1. It is only by *first* following a proper diet that many of these supplements are able to "work" to maximum effect. So I believe that these dietary changes are essential and must be primary. The supplements are really just small additions to the diet. I do not know how (or even if) these supplements – taken alone – will work for someone still consuming a typical standard American diet. Nor can I predict how well "cherrypicking" different supplements may work independently of the others. To take an example, there is now evidence that Turmeric and Resveratrol work best together synergistically. Or, in the same vein, there is recent evidence that Vitamin C allows Maitake D-fraction (a mushroom extract that can strengthen the immune system) to work much more effectively against some versions of cancers.
- 2. The diet and supplements work in two ways to allow the body's various systems to be able to work at peak efficiency. First - and foremost - is by eliminating those substances that might compromise or severely tax these internal systems. And secondly it works by increasing the presence of those substances that can

strengthen them. The basic idea is to make the body's **five interior biochemical terrains**<sup>4</sup> hostile to cancer – just as they must have been before the cancer took hold.

- 3. No diet or supplements on their own can kill or eliminate existing tumors or metastases. As such, the oncologist who believes that "only surgery or medication will be of any use" is partially correct. Without the help of a molecular targeted drug, or chemotherapy, or radiation, no diet with (or without) supplements, by itself, will be sufficient to fight cancer once it has taken hold.
- 4. Re-read caveat number 1 again.

#### IV. WHAT IS THE POINT OF ALL THIS?

So what am I trying to accomplish with this diet and its supplements? 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 otherwise healthier!
- 2. To better focus molecular targeted drugs or chemotherapy on cancer cells while minimizing their effects on normal cells.
- 3. To better tolerate targeted molecular drugs or chemotherapy and/or radiation treatments and to help minimize or prevent their unpleasant side effects.
- 4. To help prevent or minimize any future metastases.
- 5. To repair, build up, and maintain one's internal immune system by altering the body's internal "biochemical terrains". One or more of these damaged terrains has allowed cancer to take hold in the first place.
- 6. To strengthen the immune system especially if it is being compromised or weakened as a by-product of taking molecular targeted drugs, chemotherapy, or radiation.
- 7. To employ additional natural anti-angiogenic, apoptosis-inducing, and immune stimulating foods and agents in fighting tumorigenesis.
- 8. To help ensure that once going "**NED**" (**N**o visible Evidence of **D**isease) there is no return of cancer in the future.

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

<u>Note</u>: Let me just cut right to the chase. After over one year of intense research and personal experimentation I have come to the conclusion that a modified low carbohydrate / high (saturated) fat diet is the optimal approach for most cancer patients.

"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-

<sup>&</sup>lt;sup>4</sup>Credit for the concept of five internal "biochemical terrains" goes to Dr. Keith I. Block.

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."<sup>5</sup>

What follows are my arguments behind this decision.

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

#### **1.** Severely limit excess sugar(s) and starches Add sufficient fiber to help mitigate sharp insulin "spikes" due to a rapid rise in blood glucose levels

The first major area of concern in the diet is the issue of 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. This is especially true for cancer patients.

**Note**: 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 both of its forms – **sucrose** (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 Hypertension<sup>6</sup>.

<sup>&</sup>lt;sup>5</sup>Direct quote from Stephan Guyenet, from his blog: <u>http://wholehealthsource.blogspot.com/</u>

<sup>&</sup>lt;sup>6</sup>Not to mention **Insulin Resistance** (also called **IR** or **Syndrome X**) that may play a vital 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.

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.

Some critics consider his case to be lacking in sufficient evidence. But I don't agree with them and neither does Gary Taubes. He 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

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

Lustig goes on to counter the 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 fructose<sup>7</sup>. 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 is 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 an unfortunate confluence of political and economic factors that started in the early 1970's. These resulted in a misguided effort to eliminate the

<sup>&</sup>lt;sup>7</sup>Refer here: <u>http://www.nature.com/ncomms/2013/130910/ncomms3434/full/ncomms3434.html</u>

occurrence of heart disease by reducing the consumption of "fats" from 40% to 30% of 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 are sugar(s) – and again, in particular, fructose. More sugar(s) were added to mask that awful "cardboard" (flat) flavor 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**)<sup>8</sup>. It is in this detailed analysis that Lustig shows that "a calorie is not a calorie."

Glucose is a sugar that is absolutely vital to life. It is an integral part of every cells 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,

<sup>&</sup>lt;sup>8</sup>Glucose 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: ( $CH_2O$ )<sub>n</sub>.

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 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 insulin-like 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<sup>9</sup>. 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

<sup>&</sup>lt;sup>9</sup>"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 LA Times 10/22/07

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) by the gastrointestinal tract. This, in turn, prevents the sharp jump up 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 always be limited – no matter how beneficial its constituent nutrients (i.e. various phytochemicals and anti-oxidants) may actually be.<sup>10</sup>

It should be kept in mind that the brain "runs" on lots and lots of glucose. It does not run on anything else<sup>11</sup>. 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.

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:

#### 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 highsugar 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*.

<sup>&</sup>lt;sup>10</sup>This means that the "official" recommendation to "eat **5** servings of fruit a day" is actually unhealthy. <sup>11</sup>Except, that is, when the body is put into a state of nutritional **ketosis**. Brain cells can be "trained" to run off of ketones instead of glucose. Ketones are synthesized in the liver from various fatty acids.

"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 insulinresistant 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 insulinresistant 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."

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."<sup>12</sup>

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 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%.<sup>13</sup>

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. Limit consumption of milk – but cook using butter or ghee (clarified butter) or coconut oil. Never cook in vegetable oils high in poly-unsaturated fats.

There are several reasons for considering this, both science and evidence based. Still, it must be clearly stated that some of these particular recommendations are not fully resolved. For example, strident advocacy against consuming any milk and dairy

<sup>&</sup>lt;sup>12</sup>Original paper here: **"Transformed Drosophila Cells Evade Diet-Mediated Insulin Resistance through Wingless Signaling**": <u>http://www.cell.com/abstract/S0092-8674%2813%2900769-1</u>

<sup>&</sup>lt;sup>13</sup>Sanchez 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

products can be found in the book, "**The China Study**," and also in the video documentary, "**Forks Over Knives**." Yet any claimed benefits of going completely vegan remain unproven.

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

Dr. Thomas Campbell led a (flawed) 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 a 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 exactly as straightforward as they 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 or more amino acids, a scenario that rarely occurs in realworld 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 gualities 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-areview-and-critique/ Yet another critique of the flawed research and questionable conclusions reached in the book can be found here:

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

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

My major 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.<sup>14</sup>

<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 other research evidence presented in favor of a plant-based (only) diet was also very misleading and inconclusive. "The China Study" recounts a massive (but still 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 nonexistent. 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 does reveal some some tantalizing (but inconclusive) links and associations but these cannot be considered *causes*. Correlations are not causations. 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.

<sup>&</sup>lt;sup>14</sup> However, it is still not clear if consuming these growth hormones in milk can actually survive the human digestive process.

Now it may come as a shock to note that the great majority of the earth's adult population has enzyme systems that simply cannot handle milk properly. Milk gives them gas, cramps, indigestion, and may even cause emotional side effects such as depression and confusion. Note also that most children, around about 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 inflammation in all of these illnesses.

The video documentary "**Forks Over Knives**" cites an interesting example of the role of nutrition in reducing one such chronic illness. It documents a sharp reduction in Cardiovascular Disease (CVD) in the population of Norway during its occupation during World War II. After the Nazis 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 – 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, this study also sheds 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 does not come under the "limit all milk" recommendation. 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**<sup>15</sup> 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 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

<sup>&</sup>lt;sup>15</sup>Glutathione 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 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.

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, 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 all of these questions is far from clear at this point in time.

#### 3. Considerations regarding meat, fish, seafood, and the right balance of fats

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 avoid lean cuts). Fish and seafood should always figure prominently the diet (i.e. serve it at least 2 to 3 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.<sup>16</sup>

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).

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

<sup>&</sup>lt;sup>16</sup>I 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: <u>http://www.youtube.com/watch?v=rDVf-00w5gk</u> and <u>http://www.youtube.com/watch?v=F0kIC-dbW2g</u>

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, less often, 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 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 increasingly (but 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**. In fact there is now mounting evidence that lowered levels of saturated fats and/or cholesterol may 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 oil<sup>17</sup>, 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 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.

<sup>&</sup>lt;sup>17</sup>Of 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: <u>http://www.youtube.com/watch?v=omjWmLG0EAs</u>

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 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. Polyunsaturated 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 it needs. 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 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 in the diet. In the end, only a very small amount of ALA actually gets successfully converted into EPA and DHA in this 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. 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 – 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 ground flax seeds or oil, chia seeds or oil, walnuts, and pasture grass-fed beef).

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 ("SAD") it is likely to be at 20:1 or 25:1 – or even much 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 (an omega-6) has been shown to increase the oxidation of LDL 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).<sup>18</sup> Damaged fatty acids can be found in almost *all* packaged grocery items that are designed to have a long shelf life (i.e. 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,

<sup>&</sup>lt;sup>18</sup>There is one exception to the "all trans-fats are bad" rule. It does not apply to "**Conjugated Linolenic Acid**", or **CLA**. CLA is a trans-fat that is not man-made. It is made naturally in the bodies of ruminants (cows). Factory-farmed meat does *not* have any, but pasture grass-fed meat and products that come from pasture-raised animals do. CLA seems to have both anti-cancer and anti-obesity properties.

cookies, and most fast food including french fries and other fried foods. You can easily see the problem. They are still universally pervasive.

It is a fair bet that those oncologists who do not advocate paying close attention to 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.

For example, do you know who is 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. The first versions were formulated in 1869 by Hippolyte Mège-Mouriès.

Margarine is made from poly-unsaturated fats whose carbon-to-carbon double bonds have been replaced by hydrogen bonds (i.e. hydrogenated) to make them solid at room temperature. Unfortunately these new molecules are usually 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.

To sum up, poly-unsaturated fats 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 III"

"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

#### 4. Severely limit consumption of "processed" and "refined" foods

[Note: Before proceeding I wish to acknowledge my thanks to the researchers at the Block Center for Integrative Cancer Treatment for portions of the explanation that follows.]

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**<sup>19</sup> 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. 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 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

<sup>&</sup>lt;sup>19</sup>Prostaglandins 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.

Docosahexaenoic Acid (DHA) and then into the anti-inflammatory prostaglandin **PGE3**. PGE3 inhibits tumor growth, clotting, inflammation, and angiogenesis.

One of the supplements in my list is a special blend of fish oils that feature a high level of EPA.

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

[What follows is just a slight diversion to demonstrate the value of monitoring the C-RP level as a measure of internal inflammation.]

For healthy people, the optimal C-RP level is anywhere below **1.0mg/L**.

I first had my C-RP checked on September 13, 2012. This was just one month after I discovered that I had bone metastases (lytic lesions) in three areas: on my sacrum; at my T4/T5 vertebra; and my left femur. It was also just two weeks after I had first started taking the anti-angiogenic drug, Sutent (Sunitinib), at 50mg/day.

On that day my C-RP was measured to be = 44.35mg/L (Yikes!! That was downright scary). So, based on discussions with the Block Center for Integrative Cancer Treatment, we decided to try adding several supplements designed to reduce inflammation in my body. The primary supplement I added was their particular mix of fish oils called "ArcticBlox". Each ArcticBlox capsule contains 900mg of EPA and 200mg of DHA.<sup>20</sup>

One month later, on October 3<sup>rd</sup>, my C-RP level had dropped to **17.5mg/L**. This was very encouraging.

One month after that, on November 7<sup>th</sup>, my C-RP level was further reduced to **2.3mg/L**. That was great news. Normal range is considered anywhere between **1.0 to 3.0mg/L**.

However, things do not always proceed so linearly and straightforwardly when it comes to dealing with metastatic renal cancer...

One month later, on December 12<sup>th</sup>, my C-RP level showed a slight rise. It was now measured to be **3.3mg/L**. But was this significant? It was too early to speculate.

Two weeks later, on the 25th, I started to develop a diffuse throbbing pain in my left

<sup>&</sup>lt;sup>20</sup>If you have been paying attention you will note that these are both long-chain omega-3 poly-unsaturated fats that may easily be oxidized if not "protected" by anti-oxidants such as Selenium naturally found in fish. This is why it is better to get omega-3's by eating more fish and not by excess fish oil supplements.

femur (thigh). It quickly got progressively worse. More disturbingly – this was identical to the pain I had experienced back in July when mets were first discovered in that same location.

At that point in time I was just about at the end of a 2-week "break" from taking Sutent. At that time my regime had been to take Sutent at 50mg/day for 4-weeks straight followed by a 2-week break off of it. Since I was on a break, I surmised that Sutent was no longer working and my bone lesions in that area were becoming active again. I was experiencing what is known as Sutent "flare".

Sure enough, within two days of my starting back up on my next cycle of Sutent, all that pain quickly disappeared. Yet three days after that, on January 2<sup>nd</sup>, my C-Reactive Protein was measured to be **41.1mg/L**.

However, two weeks later, on January 14<sup>th</sup>, (which was now in the middle of my Sutent cycle) my C-RP had dropped back down. It was now **4.3mg/L**.

Based on this experience of Sutent flare my oncologist agreed to shorten my 2-week "vacation" break from taking Sutent to only 1-week off.

I then completed my first 1-week vacation off of Sutent and started up on my next cycle (5<sup>th</sup>). There was no repeat of any Sutent flare during that shorter 1-week break period.

On February 6<sup>th</sup> my C-RP level was measured to be down to **0.3mg/L**. That low level was completely unexpected but wonderful news indeed.

On March 8<sup>th</sup> my C-RP level was measured to be **0.7mg/L**. Note that this particular test was also done on the very last day of a 1-week vacation off of Sutent – and yet it still had not risen significantly.

On April 3<sup>rd</sup> my C-RP level was measured to be **1.4mg/L**. This test was done at the very end of a Sutent cycle.

On May 1<sup>st</sup> my C-RP level was measured to be back down to **0.7mg/L**.

However, on May 29<sup>th</sup> my C-RP level was now measured to be back up to **19.7mg/L**. This was very disconcerting. But only one week earlier, which marked the end of another one of my 1-week Sutent vacation breaks, I had started to experience some minor pain in T4/T5 vertebra area. That particular pain had already disappeared several days earlier (2 days after I had started on my next Sutent cycle.)

Regardless, 2 weeks after that, on June 14<sup>th</sup> my C-RP had dropped back down to **1.4mg/L**. This reading was taken in the middle of my 8<sup>th</sup> Sutent cycle.

But one week later I experienced yet another Sutent flare (once again at the end of my Sutent break). I began to get a bit concerned since these flares were now occurring

more and more frequently and after shorter vacation "break" periods each time. Sure enough, on June 28<sup>th</sup> my C-R P had shot back up to **15.7mg/L**. As a result my oncologist and I then decided to change my Sutent dosing and schedule. We decided to eliminate all vacation "breaks" and change my dosage to alternating between 50mg and 37.5mg every other day.

One month later, on August 1<sup>st</sup> my C-R P had dropped back down to **6.2mg/L**. But the best news of all is that my C-R P has dropped to **only 1.4mg/L** as of August 29<sup>th</sup>. This new dosing strategy is working quite well for me as of this writing (November 2013).

This short history illustrates how monthly monitoring of C-RP levels can reveal valuable information about the progression of internal tumors in between routine CT scans.

Now back to the diet...

#### 5. Limit consumption of 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 system<sup>21</sup>) 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

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

<sup>&</sup>lt;sup>21</sup>Please refer to Chapter VIII, "**TKI Interactions with Supplements and Certain Foods**" for more information on this.

"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 a process called **oxidative phosphorylation** – to primarily getting its main source of energy from the fermentation of glucose – via a 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)<sup>22</sup>.

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 is also 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 get their primary energy from the fermentation of the amino acids **glutamine** and **serine** to lactate, which has been termed

<sup>&</sup>lt;sup>22</sup>A 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**.

*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.

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 (and still is) rather controversial. The current paradigm as to the primary cause of most cancers is not what Dr. Warburg had suggested.

The 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 tumors<sup>23</sup>. 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  $F_1F_0$  ATPase).

These investigators linked their metabolic findings to defects in the von Hippel-Lindau (VHL) tumor suppressor gene and the hepatic-growth factor MET protooncogene. However, alterations in these genes alone were unable to account for

<sup>&</sup>lt;sup>23</sup>"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

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.<sup>24</sup> 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.

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.<sup>25</sup> [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

<sup>&</sup>lt;sup>24</sup>"Ibid

<sup>&</sup>lt;sup>25</sup>"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

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).

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 **ischemic**<sup>26</sup> 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<sup>®</sup>, Inlyta<sup>®</sup>, Votrient<sup>®</sup>, Nexavar<sup>®</sup>, and Avastin<sup>®</sup> work to stop tumor growth.<sup>27</sup>

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

<sup>&</sup>lt;sup>26</sup>**Ischemic** = A decrease in the blood supply to a bodily organ, tissue, or part usually caused by constriction or obstruction of the blood vessels.

<sup>&</sup>lt;sup>27</sup> Avastin® is not a TKI, it is a monoclonal antibody. However, it does target VEGF and similar receptors.

in the body.<sup>28</sup> This same premise also underlies my attempts to maintaining a consistent and normal blood glucose level with no insulin spikes.

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 fully starve most tumors because they are still able to pirate glucose at concentrations in the blood that are **way below** the normal range.

All 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 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 remains 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, Meetabolic Syndrome, etc.) and cancer progression while fueling inflammation. This can also serve to weaken the immune system. More importantly, keeping the blood 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 incidentally affect weight management and overall health.

#### A Few Other Implications to Consider:

- One should avoid consuming Gatorade<sup>®</sup> (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<sup>®</sup> 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 only "safe" beverage to relieve hydration is 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<sup>®</sup> (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 the other nutrients absorbed into the gut. Regardless, there is no

<sup>&</sup>lt;sup>28</sup>Actually, this applies to all three categories of fatty acids. The ratio of saturated fats to monounsaturated fats to poly-unsaturated fats should optimally be 1:1:1. However this can be difficult to achieve in practice.

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<sup>®</sup> (28 grams of "sugars" with no fiber) or Ensure<sup>®</sup> (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 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 per se. What would be optimum would be to consume a "timed-release" carbohydrate so as to avoid those insulin spikes. (Note that consuming adequate fiber 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 interest also have protein mixed in:

#### http://generationucan.com/super.html

- Yet another excellent source for "good" calories is pure **whey** protein. Of course this is a dairy product. But pure whey protein does not have any casein protein which is the alleged cancer-promoting agent found in milk (casein makes up to 87% of it). Pure whey should normally not have any **lactose** in it either.
- Some other common beverages that contain HFCS: chocolate milk; low fat milk; Similac<sup>®</sup>, Isomil<sup>®29</sup>, and Gatorade AM<sup>™</sup> for Kids. The bottom line: one should always beware – because sugar is everywhere (and not necessarily always noted as an ingredient on the label).

What about those diet drinks that replace the sugar with the artificial sweetener **aspartame** (also found in **NutraSweet**<sup>®</sup> and **Equal**<sup>®</sup>)? 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.

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 from following a LCHF (Low Carb/High Fat) diet:

<sup>&</sup>lt;sup>29</sup>Dr. Robert Lustig calls this stuff "a baby milkshake".

- 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 will not contribute to these unwanted events.

This ends the review of my "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 an 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.
- Ability to reduce the duration of my "break" off of Sutent from two weeks to just one and eventually to none.
- A stoppage and even reversal of atherosclerosis (calcification or hardening) that was due to plaque buildup in the walls of my arteries. For a 60-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."

#### VII. THE "APPROPRIATE" SUPPLEMENTS FOR FIGHTING CANCER

Before proceeding on to describing the supplements that I take, a few 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 any supplement taken 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 caveat that follows).
- Being completely upfront and consulting with their doctor(s) about what they are doing and why.

**VERY IMPORTANT CAVEAT**: Many of these supplements are natural anticoagulants. For anyone taking **Coumadin**<sup>®</sup> (**Warfarin**<sup>®</sup>, etc.), please do not use any of those supplements without first consulting with a medical doctor.

#### VIII. TKI INTERACTIONS WITH SUPPLEMENTS AND CERTAIN FOODS

[Note: In the following I wish to again acknowledge my thanks to the researchers at the Block Center for Integrative Cancer Treatment for the valuable insights they provided.]

There is a very serious issue in regards to ingesting any supplements (and certain foods). That issue is whether or not the substance being consumed might interfere with a 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 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**<sup>30</sup>) 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.

That is why in describing all the supplements that follow, I always post a "**SUTENT ALERT**" for those supplements (or foods) that might interact with Sutent – and in what ways they may do it.

<sup>&</sup>lt;sup>30</sup>INTERACTION OF GREEN TEA POLYPHENOL EPIGALLOCATECHIN-3-GALLATE WITH SUNITINIB: POTENTIAL RISK OF DIMINISHED SUNITINIB BIOAVAILABILITY.

My general rule is that I do 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 still do take a few supplements that "might" be *inhibitors* and could serve to increase the Sutent level. But this is only because, so far at least, I have not had any significant side effects to deal with. However, I still totally avoid grapefruit or grapefruit products<sup>31</sup> while on Sutent. These items are too unpredictable in their overall effect.

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 use 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 – energydriven, 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

OK, on to the rationale behind my list of "appropriate" supplements...

#### VIX. USE OF L-GLUTAMINE FOR GASTROINTESTINAL DISTRESS

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

This first 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 regularly. 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 (at 50mg/day). This supplement also helps to alleviate any metallic food taste as well as mouth sores, nausea, and diarrhea, etc.

<sup>&</sup>lt;sup>31</sup>Also Seville Oranges and Pomegranates or any products made from them.

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 some tumors "may" primarily feed on. 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. So 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.

**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.

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 is to eliminate free radicals in the body that can damage DNA.

### Level of Inflammation

- Which, if uncontrolled, damages cells and organs, fuels pain, discomfort, disease progression, and weakening of the immune system. I touched briefly on the results of one these tests earlier – the C-reactive protein level.

## • 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 needed to take (and at what dosage) and which might be superfluous.

Thus the supplements that I take relate directly to my own specific needs – and they are based on quantitative results from specific blood tests. These same blood tests are repeated every four months for comparison. I point all this out to underscore the fact that what works for me might turn out to be very different for others.

So here is a breakdown of the supplements that I take. It is based on the results of specific blood test "panels" related to those five key bioterrains:

# A. Terrain 1 – The Oxidation Panel

1. Blood test for Vitamin **A**, Serum (retinol) level:

Optimal value range: 18-77ug/dL.

My value on 9/13/12 = 64 ug/dL, considered good.

My value on 1/14/13 = 90ug/dL, now considered high.

My value on 6/14/13 = 91 ug/dL, still considered high.

[--The reason for a sustained high level remains unclear. A follow up check of my liver enzymes showed proper liver function. The reason may just be genetic.]

"Retinol is essential for normal cell growth and development and boosts immune function. Excess Retinol can contribute to liver, eye, skin, and bone damage. There is a need to be aware of Retinol that comes from foods of animal origin. Some fruits and vegetables contain certain carotenoids like Beta-Carotene that provide non-toxic Vitamin A activity." – Block Center for Integrative Cancer Treatment

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

Optimal value range: **12.0-46.7ug/L**.

My value on 9/13/12 = 51.1ug/L, considered high.

My value on 1/14/13 = 12.4ug/L, now considered good.

My value on 6/14/13 = 18.1ug/L, slightly higher and still good.

[--Based on the 9/13/12 test results I had stopped taking a multi-vitamin supplement. Doing this brought the value down to a good level.]

"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:

# Optimal value: 211-946pg/mL.

My value on 9/13/12 = 603 pg/mL, considered good.

My value on 1/14/13 = 273pg/mL, still considered good.

My value on 6/14/13 = 218 pg/mL, still considered good but marginal.

"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, cholesterol-lowering drugs, and potassium replacements." – Dr. Terry L. Wahls

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

Optimal value: Greater than1.2 mg/dL.

My value on 9/13/12 = 1.6 mg/dL, considered good.

My value on 1/14/13 = 0.9mg/dL, considered sub-optimal.

My value on 6/14/13 = 1.1mg/dL, considered sub-optimal but improved.

[--After the 9/13/12 blood tests I had decided to cut my dosage to 1000mg/day. But based on the 1/14/13 test I decided to go back up to 2000mg/day.]

"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 which 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

To boost this I take: Vitamin C.

Dosage = One capsule, twice a day.

One capsule = 1000mg.

**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. It was for this reason that I had initially cut my dosage in half.

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

Optimal value: 50-80ng/mL.

My value on 9/13/12 = 53.7ng/mL, considered good.

My value on 1/14/13 = 58.6ng/mL, still considered good.

My value on 6/14/13 = 45.0ng.mL, considered sub-optimal.

"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  $Oren^{32}$ : "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) twice a day.

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

**Note**: 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.

Due to my taking Xgeva (denosumab) I also take: Calcium Citrate + Magnesium. Dosage: One capsule once a day.

One capsule = 500mg Calcium Citrate; 200mg Magnesium Aspartate.

This supplement is absolutely essential for building up calcium in the bloodstream while taking Xgeva (denosumab).

**Note**: Calcium Citrate, Calcium Ascorbate, and Calcium Hydroxyapatite can all be digested easily but Calcium Carbonate cannot.

"Magnesium blocks excessive stimulation from glutamate...[it] has been shown to be helpful in reducing the severity of tension headaches and migraines and has been shown to be neuroprotective in animal models of brain injury. Because people eat so few green leafs, and because stress tends to cause magnesium wasting, many Americans are relatively depleted in their magnesium stores. Good sources include pumpkin seeds, sesame seeds, sunflower seeds, spinach, Swiss chard, black beans, and pinto beans...The primary side effect from excessive magnesium is diarrhea." – Dr. Terry L. Wahls

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

Optimal value: Greater than 9.4mg/L.

My value on 9/13/12 = 23.8mg/L, considered too high.

My value on 1/14/13 = 15.9mg/L, now considered good.

My value on 6/14/13 = 20.5mg/L, considered elevated.

[--Based on the 9/13/12 result I had stopped taking a multi-vitamin supplement. This brought the value down into the good range.]

"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<sub>10</sub>** level:

Normal range: 0.37-2.20ug/mL.

Optimal value: Greater than 1.3ug/mL. My value on 9/13/12 = 3.88ug/mL, considered good but high. My value on 1/14/13 = 6.52ug/mL, still considered good but high. My value on 6/14/13 = 6.24ug/mL, still considered good but high. [--The 1/14/13 value could be reduced so I cut the dosage in half – to only 200mg/day. The 6/14/13 level can still be reduced so will cut the dosage to only 100mg/day].

**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<sub>10</sub> deficiency can affect the heart as profoundly as a calcium deficiency can affect the bones. CoQ<sub>10</sub> also has the ability to reduce blood pressure. And it is a very potent intracellular anti-oxidant.

**<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<sub>10</sub> 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  $Q_{10}$ ] 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

**Important Note for anyone taking Xgeva or Zometa**<sup>®</sup>: 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 jaw bone 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**<sup>®</sup>); alendronate (Fosamax<sup>®</sup>); risedronate (Actonel<sup>®</sup> and Atelvia<sup>®</sup>); ibandronate (Boniva<sup>®</sup>); and denosumab (**Xgeva<sup>®</sup>** and Prolia<sup>®</sup>). 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 CoQ<sub>10</sub> 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 CoQ<sub>10</sub> level I take: **Ubiquinol**.

Dosage: 1 capsule once a day.

One capsule = 100mg Ubiquinol (CoQH – this is the active form of  $CoQ_{10}$  - Ubiquinone).

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

Optimal value: Greater than 12.0ng/mL.

My value on 9/13/12 = 19.9ng/mL, considered good.

My value on 1/14/13 = 13.2ng/mL, still considered good.

My value on 6/14/13 = 13.3 mL, still considered good.

"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 hyperhomocysteinemia, 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:

Optimal value: **95-134ug/dL**. My value on 9/13/12 = 102ug/dL, considered good. My value on 1/14/13 = 101ug/dL, still considered good. My value on 6/14/13 = 89ug/dL, considered sub-optimal. [--The 6/14/13 value needs to be boosted so I will start taking a 50mg daily supplement.] "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 pro-inflammatory 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

To maintain an optimal Zinc level I take: **Zinc**. Dosage: 1 capsule once a day. One capsule = 50mg Zinc.

## B. Terrain 2 – The Inflammation Panel

 Blood test for C-Reactive Protein – Highly Sensitive level: Normal value = 1.0-3.0mg/L. Optimal value = Less than 1.0mg/L. My value on 9/13/12 = 44.0mg/L, considered extremely high. My value on 10/3/12 = 17.5mg/L, considered high. My value on 11/7/12 = 2.3mg/L, considered normal. My value on 12/12/12 = 3.3mg/L, considered high. My value on 1/2/13 = 41.1mg/L, considered extremely high. My value on 1/14/13 = 4.53mg/L, considered high. My value on 2/6/13 = 0.3 mg/L, considered optimal. My value on 3/8/13 = 0.7 mg/L, considered optimal. My value on 4/3/13 = 1.4mg/L, considered normal. My value on 5/1/13)= 0.7mg/L, considered optimal. My value on 5/29/13 = 19.7mg/L, considered high. My value on 6/14/13 = 1.4mg/L, considered normal. My value on 6/28/13 = 15.7mg/L, considered high. My value on 8/1/13 = 6.2 mg/L, considered high. My value on 8/29/13 = 1.4mg/L, considered normal. My value on 9/26/13 = 1.6mg/L, considered normal. My value on 10/17/13 = 1.7mg/L, considered normal.

[--My initial C-R P test was done on 9/14/12. The number was so disturbingly high that I decided to repeat this particular blood test every month since. As noted earlier, my reading in November 2012 showed that it had dropped down to **2.3mg/L**. At the time I had attributed this huge drop as mostly due to my diet and supplements such as fish oil. However, in light of my further experience while dealing with Sutent "flare" around Christmas 2012 and since, it has became clear to me that the combination of Sutent + Xgeva is likely the major reason for my low inflammation and C-R P readings.]

"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:

Optimal value: Less than 5.0pg/mL. My value on 9/13/12 = 3.5pg/mL, considered good. My value on 1/14/13 = 2.5pg/mL, still considered good.

My value on 6/14/13 = 2.1 pg/mL, still considered good and improved.

"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:

Optimal value: Less than 984ng/mL.

My value on 9/13/12 = 720ng/mL, considered good.

My value on 1/14/14 = 390ng/mL, still considered good.

My value on 6/14/14 = 196 mg/mL, still considered good and improved.

"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

I am currently taking four supplements that help to lower Inflammation:

# a. Ayur-Boswellia Serrata (also called Indian Frankincense)

Dosage: Four capsules twice a day - not taken with food. One capsule = 200mg.

"Boswellia has been shown to aid in inflammatory conditions such as Inflammatory Bowel Syndrome and Asthma. Boswellic Acids inhibit **5-Lipoxygenase** (**5-LOX**) and leukotriene synthesis, and inhibit leukocyte elastase, which are the likely mechanisms for its anti-inflammatory properties." – Block Center for Integrative Cancer Treatment

**SUTENT ALERT**: This supplement tends to inhibit CYP3A4 based on lab studies, which could increase the Sutent concentration.

I now take a better supplement than **Boswellia**. It is called **Scutellaria** (**Standardized Scut**):

Dosage: Two capsules once daily with or without food.

### One capsule = 420mg.

"The flavonoid compounds of scutelleria (baicalin, baicalein, and wogonin) contain significant anti-inflammatory and antioxidant effects...scutelleria contains some of the most exciting anti-aging and healthy inflammation response molecules known to science. Interestingly, baicalin is one of the only known naturally occurring compounds with 12-LOX modulatory activity. This makes scutelleria a key therapy for promotion of normal cell growth in multiple tissue types within the prostate, brain, pancreas, bladder, breast, liver, colon, and gastric system...moreover, scutelleria provides immune support, promotes relaxation without a sedating effect, modulates histamine release, and offers protection to healthy cells during oxidative treatments." – Block Center for Integrative Cancer Treatment

## b. Resveratrol - Advanced Resveratrol Formula

Dosage: 2 tablets, twice a day.

One tablet = 150mg Red Grape (Vitis Vinifera) Seed; 150mg Red Grape (Vitis Viifera) Skin; 100mg Red Wine (Viti Vinifera) Dried Extract; 100mg Japanese Knotweed (Polygorum Cuspidatum) Root; 500mg Citrus Bioflavanoid Complex; 25mg Quercetin.

[<u>Note</u>: 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 antimutagenic, anti-inflammatory, and anti-oxidant activities. Due to its potent antioxidative 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.

# c. ArcticBlox - Maximum Strength EPA

Dosage: 2 Softgels twice a day.

2 Softgels = 1200 mg Omega-3 Fatty acids: EPA = 900mg; DHA = 200mg; other = 100mg.

"ArcticBlox is the Block Center's highly concentrated Omega-3 fish oil... Although EPA and DHA are made within the body from another Omega-3 fatty acid, Alpha-Linolenic Acid (ALA) commonly found in Flax, the conversion of ALA to EPA and DHA is very inefficient. Taking Omega-3 fish oil in softgel or liquid form facilitates intake at higher levels than those achieved by fish consumption alone... EPA and DHA inhibit a number of steps in the carcinogenic process... they can also aid in cardiovascular function and have anti-inflammatory benefits." – Block Center for Integrative Cancer Treatment

# d. Phytosome Turmeric - Liposomal Curcumin

Dosage: 2 capsules twice a day.

One capsule = 500mg Meriva Turmeric Phytosome (Curcuma Longa Rhizome/Glycine Max Soybeans).

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 = diferuloyImethane) 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<sup>®</sup>) 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: <u>http://www.ncbi.nlm.nih.gov/pubmed/17569207</u>

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

**Note**: There is also evidence of a strong synergistic relationship between Curcumin and Resveratrol when taken together.

**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:

Optimal value: Less than 350mg/dL.

My value on 9/13/12 = 500 mg/dL, considered high.

My value on 1/14/13 = 474mg/dL, still considered high.

My value on 6/14/13 = 291 mg/dL, now considered good.

"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:

Optimal value: 87-325pmol/L.

My value on 9/13/12 = 848pmol/L, considered high.

My value on 1/14/13 = 524pmol/L, considered high.

My value on 6/14/13 = 427 pmol/L, still considered high but improved.

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

In addition to **Scutelleria** (mentioned earlier) I am currently taking one other supplement to help ease blood flow and circulation:

# Nattokinase II

Dosage: Three caplets twice a day.

One capsule = 50mg.

"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

**Note**: 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:

Optimal value: **2.6-24.9ulu/mL** (while fasting). Optimal value: **15-39.9ulu/mL** (while non-fasting). My value on 9/13/12 = 30.1ulu/mL, considered good. My value on 1/14/13 = 6.1ulu/mL, still considered good. My value on 6/14/13 = 2.4ulu/mL, considered very good. [--The 9/13/12 test was done non-fasting.]

**Fasting Blood Glucose** levels (unable to explain these high readings): Optimal value = **70-105mG/dL** (while fasting). My value on 10/3/12 = 105mG/dL, considered normal (but just barely). My value on 2/6/13 = 108mG/dL, now considered slightly high. My value on 3/8/13 = 115mG/dL, considered slightly high. My value on 4/3/13 = 107mG/dL, considered slightly high. My value on 5/1/13 = 122mG/dL, considered very high. My value on 5/29/13 = 112mG/dL, considered slightly high. My value on 6/28/13 = 108mG/dL, considered slightly high. My value on 8/1/13 = 105mG/dL, considered slightly high. My value on 8/29/13 = 105mG/dL, considered normal (but just barely). My value on 8/29/13 = 107mG/dL, considered slightly high. My value on 9/12/13 = 98mG/dL, considered normal. <sup>33</sup> My value on 10/17/13 = 98mG/dL, considered normal.

My **Hemoglobin A1c** level on 5/29/13 = 5.3%, considered good. My **Hemoglobin A1c** level on 9/12/13 = 4.94%, considered good. 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.

What these tests clearly demonstrate is that I have successfully reversed chronic insulin resistance simply by changing to a low carb/high fat diet.

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

Optimal value: **1.1-2.0ng/mL** (while fasting). Optimal value: **2.0-4.4ng/mL** (while non-fasting). My value on 9/13/12 = 7.4ng/mL, considered high. My value on 1/14/13 = 2.9ng/mL, considered high but improved. My value on 6/14/13 = 1.7ng/mL, now considered good. [--The 9/13/12 test was done non-fasting.]

<sup>&</sup>lt;sup>33</sup>Previous high levels may have been due to drinking a cup of dark coffee (due to its caffeine content) the morning of the blood tests. Caffeine can cause an adrenaline spike that in turn will increase blood glucose levels.

"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:

Optimal value ranges by **Body Mass Index (BMI)**. My BMI = **23.7**, considered ideal. For that BMI, optimal Leptin value: **0.2 - 8.6ng/mL**. My value on 9/13/12 = Less than 0.5ng/mL, considered low. New BMI = **21.9**, still considered ideal:

My value on 1/14/13 = 3.3ng/mL, now considered good.

My value on 6/14/13 = 1.1 mg/mL, still considered good.

"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 is between **51 to 194ng/mL**.

My value on 9/13/12 = 121 mL, considered good.

My value on 1/14/13 = 156ng/mL, still considered good.

My value on 6/14/13 = 107ng/mL, still considered good.

"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 142 lbs. My minimum is not to go below 140 lbs.

I also try to keep a constant blood sugar level by consuming small frequent meals (or snacks) every 3 to 4 hours and 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 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:

Optimal value: **136-406/uL**.

 $\dot{My}$  value on 9/13/12 = 42/uL, considered very low.

My value on 1/14/13 = 131/uL, much better, slightly sub-optimal.

My value on 6/14/13 = 127/uL, still slightly sub-optimal.

"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:

Optimal value: 801-2402/uL.

My value on 9/13/12 = 1274/uL, considered good.

My value on 1/14/13 = 864/uL, still considered good.

My value on 6/14/13 = 1047/uL, considered good and now improved.

"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-PD-1 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:

Optimal value: Less than 15.1ugEg/mL.

My value on 9/13/12 = 12.8 ugEg/mL, considered good.

My value on 1/14/13 = 15.2ugEg/mL, considered slightly high.

My value on 6/14/13 = 13.3ugEg/mL, considered good once again.

"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

I currently take two supplements specifically designed to boost my immune system. However, there are several other supplements that, while primarily geared to protecting either the kidney or liver (or both), also boost the immune system. They are described here as well:

#### a. Melatonin P.R. (Prolonged Release) Dosage: 6 pills orally at night before bed. One pill = 3mg.

Slowly work up to the goal of 18mg/dose (6 pills). Melatonin works during the nighttime hours and also regulates the sleep cycle. It is **mTOR2** blocker (so is **Metformin**).<sup>34</sup>

"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.

4. Myco Essentials

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

Dosage: 2 tablets twice a day.

3 tablets = Proprietary Blend 2250mg: LEM (Shiitake Mycelia extract) – 20:1; Red Reishi fruiting body extract – 15:1; Maitake fruiting body extract –  $10:1^{35}$ ; Coriolus Versicolor – 7.5:1; Agaricus Blazeii – 4:1; Cordyceps Mycelia – 4:1.

"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

The supplements that I take that primarily protect the kidney or liver:

<sup>&</sup>lt;sup>34</sup>Afinitor (Everolimus) is an **mTORC1** blocker.

 <sup>&</sup>lt;sup>35</sup>Unpublished studies (by Dr. Sensuke Konno – NY Medical College) state that Maitake D-fraction may work synergistically with vitamin C to induce apoptosis in certain tumors.
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5. Astragalus.

Dosage: One capsule twice a day.

One capsule = 500mg Astragalus Extract.

This is primarily for kidney health. It has been found to be highly effective against renal cancer. It is extracted from a Chinese root.

**SUTENT ALERT**: This one tends to increase the activity of the CYP3A4 enzyme. This could lead to a decrease in Sutent concentration. This warning is based on lab studies only and not in humans – so it is not that reliable. Regardless I only take Astragalus during my Sutent break.

6. Milk Thistle (Silybum Marianum)

Dosage: Two capsules twice a day.

One capsule = 250mg.

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.

7. N-Acetyl Cysteine (NAC) II

Dosage: One capsule, twice a day.

One capsule = 500mg.

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

Ultra-Lipoic Forte (alpha lipoic acid).
 Dosage: 2 capsules, twice a day.
 One capsule = Alpha-Lipoic Acid 1,000mg.
 This is taken primarily to help protect the kidney.

"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 I 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.

This completes my list of supplements – except for one rather unique and important one. It qualifies under a category all by itself:

# 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 started on. This may be significant because it seemed to have had a noticeable effect **prior to** my starting on Sutent and the other supplements in my list:

# 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.

It recently received FDA approval as an "orphan drug" for the treatment of Multiple Myeloma.

It also recently completed its first Phase II Clinical Trial:

http://abstracts.hematologylibrary.org/cgi/content/abstract/116/21/5042?maxtoshow= &hits=10&RESULTFORMAT=&fulltext=sea+cucumber&searchid=1&FIRSTINDEX=0 &volume=116&issue=21&resourcetype=HWCIT

And it seems that more trials are either underway or planned.

Here are some earlier studies about it:

http://abstracts.hematologylibrary.org/cgi/content/abstract/118/21/5109?maxtoshow= &hits=10&RESULTFORMAT=&fulltext=tbl-12&searchid=1&FIRSTINDEX=0&sortspec=relevance&resourcetype=HWCIT

http://www.ncbi.nlm.nih.gov/pubmed/15645493

These links (from Australia) may also shed some light on it:

http://www.unicorn-pacific.com/tbl\_1.html

http://www.unicorn-pacific.com/specs\_1.html

http://www.unicorn-pacific.com/documents/index.html

**SUTENT ALERT**: There is no published data available on how TBL-12 is metabolized.

# G. My TBL-12/Sea Cucumber Experience

On July 31, 2012 my oncologist confirmed that I was no longer NED. Mets were discovered on my sacrum (base of my spine) and my left femur (hip/thigh). On that same day, after almost 60 years of eating a typical western diet, I resolved to give up most meat (excepting fish and seafood) and dairy products. The next day I received my first shot of Xgeva (denosumab), however, I did *not* start taking any Sutent quite yet.

Around this time I began to develop a dull, throbbing pain in my left thigh. It progressively got worse and worse. I was soon walking with a limp and I could no longer go up the stairs normally – I could only manage one feeble step at a time. The pain was progressively getting worse and it would completely fatigue me. I would spend most of Copyright © 2013 Neil B. Feldman Page 56 11/10/13

my day flat on my back. I could only control this pain by taking the maximum dosage of Ibuprofen (400mg) every 6 hours. This, of course, was absolutely the worst thing to do for the kidney – but I found that acetaminophen (which is metabolized by the liver) had no effect on this pain at all. I really thought I was a goner – since I had gone downhill so quickly.

On August 10<sup>th</sup> (some 10 days later) I began taking daily doses of TBL-12/Sea Cucumber. I still had not started on Sutent or any other supplements yet.

On August 18<sup>th</sup> I started taking some of the other supplements in my list.

On August 24<sup>th</sup> I started on my first dose of Sutent (50mg). Interestingly, the very next day, August 25<sup>th</sup>, my pain started to subside. By August 28<sup>th</sup> I was completely pain free and have been ever since (except during my 3 subsequent Sutent flare episodes).

So what, exactly, led to the end of all my pain so quickly? Looking back I now conclude that it was the combination of diet, supplements, Sutent, and Xgeva - but not the TBL/12.

**FURTHER UPDATE**: On February 15, 2013 I stopped taking TBL-12/Sea Cucumber. The reason was that it was just too expensive to justify. After I stopped taking it I can now report that there was no difference in my overall health. So taking TBL-12 was not the reason behind why I have not experienced any fatigue to date.

On that note I have completed my explanation of the rationale and science behind what I personally am doing.

I have tried to compress a vast array of research - and at times 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.

### XI. SOME FINAL THOUGHTS

Eric Jacobs, a senior epidemiologist and vitamin specialist with the American Cancer Society, once wrote: "There is no vitamin or mineral supplement proven to reduce the risk of cancer."

I hope that I have proven this sentiment to be misguided. It is way past the time to stop being close-minded and to reconsider the role of proper nutrition and appropriate supplements in helping to prevent or combat all forms of cancer.

Always try to keep in mind these conclusions from "Cancer as a Metabolic Disease":

- 1. Lifestyle changes can help manage and prevent cancer.
- 2. Most cancer, regardless of cell or tissue origin, is 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 do not have a growth advantage over normal cells.
- 7. Cancer cells depend largely on glucose and glutamine metabolism for survival, growth, and proliferation.
- 8. Restricted access to glucose and glutamine may compromise cancer cell growth and survival.
- 9. Protection of mitochondria from oxidative damage can 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.

Any questions, thoughts, or suggestions please feel free to contact me at:

Neil Feldman 240-793-0427 (cell) n.feldman@videopost.com

[Began diet modifications on 7/31/12; Xgeva<sup>®</sup> on 8/1/12; Supplements on 8/18/12; Sutent<sup>®</sup> on 8/24/12]

#### XII. APPENDIX A - SUPPLEMENTS SORTED IN ALPHABETICAL ORDER:

## 1. Advanced Resveratrol Formula

- Dosage: 2 tablets, twice a day. One tablet = 150mg Red Grape (Vitis Vinifera) Seed; 150mg Red Grape (Vitis Viifera) Skin; 100mg Red Wine (Viti Vinifera) Dried Extract; 100mg Japanese Knotweed (Polygorum Cuspidatum) Root; 500mg Citrus Bioflavanoid Complex; 25mg Quercetin.
- Rationale: To help protect kidney. In vitro and animal studies with Resveratrol and Grapeseed extract (another ingredient) shows it is effective in killing tumors as a natural anti-angiogenesis agent.
- **SUTENT ALERT**: This tends to inhibit CYP3A4, which would increase the Sutent concentration.

## 2. ArcticBlox - Maximum Strength EPA

Dosage: 2 Softgels once a day. 2 Softgels = 1200 mg Omega-3 Fatty acids: EPA = 900mg; DHA = 200mg; Other = 100mg.

Rationale: To reduce inflammation and high C-reactive protein number. May also protect against hypertension since it tends to lower blood pressure. Maintain proper Omega-3 ratio.

## 3. Ayur-Boswellia Serrata (also known as Indian Frankincense)

Dosage: Four capsules twice a day, on empty stomach. One capsule = 200mg.
 Rationale: To prevent inflammation. It is a powerful natural anti-inflammatory agent.
 SUTENT ALERT: This tends to inhibit CYP3A4 based on lab studies, which would increase the Sutent concentration.

# However, there is a better alternative to **Boswellia**:

### Scutellaria (Standardized Scut):

Dosage: Three capsules twice daily with or without food. One capsule = 420mg.

# 4. Calcium Citrate Plus Magnesium

Dosage: One capsule once every other day. One capsule = 500mg Calcium Citrate/200mg Magnesium Aspartate.

Rationale: Essential for building up calcium in the blood/bones when taking XGEVA. <u>Note</u>: Do NOT take Calcium Carbonate. Only Calcium Citrate, Ascorbate, or Hydroxyapatite can be metabolized in the gut.

# 5. Fiber Capsules

Dosage: Two capsules once a day in morning. One capsule = .52g Psyllium Husk. Rationale: To insure a minimum amount of soluble fiber is always in my digestive system.

# 6. L-Glutamine

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

Rationale: Well known for its digestive and gastrointestinal support. Reduces the side effects of harsh chemo treatments. Combats loss of taste, mouth soreness, and any gastrointestinal distress while taking Sutent.

ALERT: Only take L-Glutamine IF gastrointestinal side effects cannot be managed. Copyright © 2013 Neil B. Feldman Page 59 11/10/13

### 7. Melatonin P.R. (Prolonged Release)

Dosage: 6-3mg/pills orally at night - slowly work up to a **goal of 18mg/dose** (6 pills). Rationale: A few different studies in vivo show cancer benefit at a dose more along

the lines of 20mg or 30mg orally. It works during the nighttime hours.

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

### 8. Milk Thistle

Dosage: Two capsules once a day.

Rationale: This is for liver health. This is an herb native to the Mediterranean that has been used for centuries to support liver function.

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

### 9. Myco Essentials - proprietary blend of Mushroom Extracts

Dosage: Two capsules twice a day.

Rationale: To help boost the Immune system. This is a potent blend of 6 medicinal Mushroom extracts that work synergistically to activate and support the immune system. Can also provide critical support during chemo and radiation therapy while guarding against treatment induced side effects. These multiple mushroom extracts also tend to have mild blood-thinning effects.

## 10. N-Acetyl Cysteine (NAC) II

Dosage: One capsule once a day. One capsule = 500mg.

Rationale: To help protect the kidney. Powerful anti-oxidant. Biologically active precursor for the amino acid cysteine which, in turn, is a precursor for Glutathione, a tripeptide with antioxidant properties.

### 11. Nattokinase II

Dosage: Three caplets twice a day. One capsule = 50mg.

Rationale: Protects against blood clots. This is an enzyme isolated from Natto, a traditional Japanese fermented Soy product. It supports heart health and promotes healthy circulation. It regulates Blood Pressure. It is also a fibrinolytic enzyme that decreases platelet aggregation. It is favored over Bromelain.

### 12. Phytosome Turmeric - Liposomal Curcumin

Dosage: 2 capsules twice a day. One capsule = 500mg Meriva Turmeric Phytosome (Curcuma Longa Rhizome/Glycine Max Soybeans).

Rationale: To reduce inflammation. Also decreases chemo side effects and potentiates it. Turmeric is recognized as the single most potent anti-inflammatory and anti-cancer spice commonly available.

**SUTENT ALERT**: No effect in human studies but animal studies show it tends to inhibit CYP450 3A4 on humans, which would increase the Sutent concentration. It also tends to inhibit P-Glycoprotein.

### 13. Ubiquinol

Dosage: 1 capsule once a day. One capsule = 100mg Ubiquinol.

Rationale: Helps to protect the heart. There are nearly 40 anecdotes historically

of coenzyme Q10 - CoQ10 (Ubiquinone) remitting or improving cancer. Ubiquinol (CoQH) is the active form of CoQ10. Everyone is deficient in this.

### 14. Vitamin C – Solaray Two-Stage, Timed Release (Solaray slr4451)

Dosage: 1 capsule once a day. One capsule = 1000mg.

Rationale: Intravenous Vitamin C has studies that show some benefit. Liposomal C cannot reach those blood levels though. However, anecdotally, this stuff is vitamin C on steroids.

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

## 15. Vitamin D3 + Vitamin K2 - Liposomal

Dosage: 2000 units (2 sprays) once a day. Hold liquid under tongue for 30 seconds. One spray = 1000IU Vitamin D3; 100mcg Vitamin K-2.

Rationale: Essential when taking Xgeva to maintain source of Calcium in bloodstream. Many studies correlate higher vitamin D with less cancer incidence and better prognosis. A study showed that cancer patients are like 15% less likely to die in the "bright" 6 months of the year rather than the other 6 months. This suggests that sunlight improves outcomes. A map of cancer incidence in the US shows that it goes down the closer you get to the equator, also indicating that sunlight helps.

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

### 16. Ultra-Lipoic Forte

Dosage: 2 capsules twice a day. One capsule = Alpha-Lipoic Acid 1,000mg.

Rationale: Helps protect kidney. This is a non-vitamin coenzyme that carries out important metabolic and antioxidant functions in the body. Plays an important role in blood glucose disposal. It also scavenges a number of free radicals and helps the body regenerate Glutathione. However, it has been found to inhibit CYP3A4 enzyme and thus it may interfere with action of Sutent.

**SUTENT ALERT**: This inhibits NADPH – Cytochrome P450 Reductase. This enzyme supplies the electrons (energy) for CYP 450 reactions. If there are not enough electrons the CYP enzymes will not be able to act and thus will be inhibited. When they are inhibited they will tend to make the Sutent concentration increase.

#### XIII. APPENDIX B - ABRIDGED DIETARY GUIDELINES:

#### Items to restrict or totally avoid:

- 1. No sugar(s) or sugar substitutes such as aspartame. Small amounts of stevia or xylitol are acceptable. No agave (its mostly fructose).
- 2. No sodas, fruit juices, or sweetened beverages with added sugars or HFCS.
- 3. Try to limit beef and lamb to pasture grass-fed sources.
- 4. Try to limit pork to those that are organic, hormone and antibiotic-free fed.
- 5. Try to limit chicken to those that are cage-free, hormone and antibiotic-free fed.
- 6. Try to limit eggs to those from cage-free chickens fed with organic, hormone and antibiotic-free feed (they have the highest percentage of omega-3 fats).
- 7. Limit dairy or dairy products such as: Milk; Cheese; Yogurt; Sour Cream; Cottage Cheese. However, cooking in butter (or coconut oil) is encouraged.
- 8. No trans-fats: 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.
- 9. No "low-fat" versions of food (they generally have high levels of sugars).
- 10. No processed meats (i.e. nitrate-preserved or cured bologna, salami, sausage, bacon, etc.)
- 11. Limit cured, salted, or smoked foods.
- 12. Limit processed foods or those packaged with chemical preservatives.
- 13. Limit any foods whose fiber has been reduced or totally removed.
- 14. Do not cook in vegetable oils such as Canola, Corn, Sunflower, Safflower, Soybean, etc. [Cook in butter in coconut oil.]
- 15. Avoid high temperature, long period heating or cooking in olive oil. Use cold pressed, unrefined (extra virgin) olive oil.
- 16. Try to avoid all fried foods.
- 17. Limit alcohol (ideally no more than the equivalent of 2 glasses of wine; always drink alcohol with food).
- 18. No refined or processed carbohydrates such as found in packaged goods: crackers, cereals, potato (or other) chips, etc.
- 19. No white potatoes (and limit amount of red or sweet potatoes).
- 20. No white (flour) breads, pastas, etc. If necessary, substitute real whole grain products such as Ezekiel 4:9 breads.
- 21. Limit white rice.
- 22. Limit Tofu that is made with casein protein (i.e. with milk).
- 23. Limit citrus fruits (but lemons and limes are OK).
- 24. Limit pickled foods.
- 25. Green tea should be consumed only after one week off of taking Sutent.
- 26. No Grapefruit (or products made from them) while taking Sutent.
- 27. No Seville Oranges (or products made from them) while taking Sutent.
- 28. No Pomegranates (or products made from them) while taking Sutent.

### Items to consume more of:

- 1. Pure clean water.
- 2. Try to have fish or seafood at least 3 or 4 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).

- 3. Small fish have the least amount of heavy metals. Consider canned sardines, anchovies, mackerel, and tuna (chunk light versions, not albacore).
- 4. Organically grown veggies: Spinach, Celery, Carrots, Beets, Squash, Swiss Chard, Brussel Sprouts, Kale, Onions, etc.
- 5. Raw nuts: Walnuts, Almonds, and Pecans. Nothing roasted. Keep nuts refrigerated and in the dark after opening their containers. Go easy on cashews and limit peanuts
- 6. Colored fruits all berries and cherries, etc.
- 7. Avocado.
- 8. Fresh mushrooms, especially Shiitake, Maitake, and Reishi. [But note that their anti-cancer fighting compounds may not be fully metabolized].
- Dried beans (canned beans not recommended due to additional of salt, preservatives, and BPA lining). But be careful – legumes can have a high glycemic index.
- 10. Quinoa.
- 11. Humus.
- 12. Boil, bake, or steam foods is preferred; eating raw is the best.
- 13. Cocoa flavanols –dark chocolate of at least 65% cocoa (2 squares max. per day)
- 14. Turmeric spice.
- 15. Fresh Garlic.
- 16. Green tea (2-3 cups) but only after one week off of **taking Sutent**.

### Items that are not food:

- 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.

#### XIV. APPENDIX C - SUPPLEMENTS THAT I NO LONGER USE:

#### 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

Dosage: One capsule twice a day. One capsule = 500mg Astragalus Extract.

**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. lodoral.

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 Vitamins

Block Integrative Cancer Center suggested my stopping this due to high Vitamin E and B6 levels.

#### 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.

#### 11. TBL-12 - Sea Cucumber/Sargassum/Sea Sponge/Shark Fin/Sea Urchin

This extract acts as a natural anti-angiogenesis agent with broader targets than in Sutent. It has just received approval from the FDA as an "orphan drug" for treating Multiple Myeloma.

Reason for stopping: It is extremely expensive **and it** remains unknown as to how it is metabolized.