Brian Johnson's PhilosophersNotes
More Wisdom in Less Time

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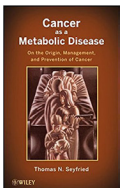

Cancer as a Metabolic Disease

On the Origin, Management, and Prevention of Cancer

BY THOMAS SEYFRIED · WILEY © 2012 · 438 PAGES

"Cancer persists as a plague in modern society. The lack of progress in either managing or preventing cancer motivated me to write this treatise. I am a biochemical geneticist and have worked on the lipid biochemistry of cancer since the early 1980s. I have developed numerous mouse models for brain tumors and for systemic metastatic cancer. Several major findings planted the seed for this treatise. First, it became clear to me that the therapeutic action of some anticancer drugs operated largely through reduced calorie intake. Second, that reduced caloric intake could target the majority of cancer hallmarks. Third, that ketone bodies can serve as alternative fuel to glucose in most cells with normal respiratory function. Fourth, that metastatic cancer arises from cells along macrophage lineage. Fifth, that all cancer cells regardless of tissue origin express a general defect in mitochondrial energy metabolism. Finally, that cancer can be effectively managed and prevented once it becomes recognized as a metabolic disease.

In recognizing cancer as a metabolic disease, it gradually became clear to me why so many people die from the disease. Many of the current cancer treatments exacerbate tumor cell energy metabolism, thus allowing the disease to progress and eventually become unmanageable. Most cancer patients do not battle their disease but are offered toxic concoctions that can eventually undermine their physiological strength and their will to resist. Cancer treatments are often feared as much as the disease itself. The view of cancer as a genetic disease has confounded the problem and is largely responsible for the failure to develop effective therapies. The view of cancer as a genetic disease is based on the flawed notion that somatic mutations cause cancer. Substantial evidence indicates that genomic instability is linked to protracted respiratory insufficiency. Once cancer becomes recognized as a metabolic disease with metabolic solutions, more humane and effective treatment strategies will emerge. My treatise highlights cancer as a metabolic disease and identifies the inconsistencies of the gene theory of cancer. Moreover, my treatise addresses most of the so-called provocative questions raised by the National Cancer Institute regarding outstanding issues in cancer research. This treatise lays the foundation for the eventual resolution of the disease."

~ Thomas Seyfried from *Cancer as a Metabolic Disease*

"The data in Table 1.1 shows that we are not winning the war on cancer, regardless of what the pundits say. ... When will this continuum end? It will end, in my opinion, only after we come to recognize cancer as a metabolic disease that can be effectively managed with nontoxic metabolic therapies. My goal is to provide scientific evidence supporting this view."

~ Thomas Seyfried

This is our eight Note on cancer books. We started with *Anticancer* then *Tripping over the Truth* then *The Metabolic Approach to Cancer* then *Cancer as a Metabolic Disease* (the journal article) then *Keto for Cancer* then *Outside the Box Cancer Therapies* then *Radical Remission*.

This is also our second Note on Thomas Seyfried's work. We started with the journal article also called "Cancer as a metabolic disease." That 22-page, peer-reviewed journal article (7 pages of which are references) lays out the scientifically rigorous, intellectual framework for

" Emerging evidence suggests that cancer is primarily a metabolic disease rather than a genetic disease. I will present evidence showing how cancer is a disease of defective cellular energy metabolism and that most of the genomic defects found in cancer arise as secondary downstream effects of defective energy metabolism."

~ Thomas Seyfried

our metabolic protocol to conquering cancer—mapping out why cancer is, as the title suggests, primarily a METABOLIC disease (vs. a genetic disease).

I HIGHLY recommend you print that out. Go to quiet place. Read it. Mark it all up. Wrap your brain around it. Then share it with your oncological team and interested family and friends and then, most importantly, go rock your metabolic therapy based on this theoretical approach.

(Note: I traded emails with Professor Seyfried midway through the creation of this Note. He shared two other newer articles he highly recommends as well: A 2015 journal article from *Frontiers in Cell and Developmental Biology* called *Cancer as a mitochondrial metabolic disease* and a 2017 article from *Nutrition & Metabolism* called *Press-pulse: a novel therapeutic strategy for the metabolic management of cancer.*)

After reading those, if you're *really* feeling it, go deep with this 421-page, textbook-like treatise.

Seyfried has taught and conducted research in the fields of neurogenetics, neurochemistry and cancer for more than twenty-five years at Yale University and Boston College. He is the leading scientist pointing to (and nearly screaming at!) the SUPER-compelling evidence that says cancer is caused by dysfunctional *energy metabolism*—providing evidence that the genetic mutations are a secondary, downstream epiphenomenon of that primary cause.

I firmly believe that if the National Cancer Institute focused its $5 BILLION (!!!) annual budget on ideas in this book and the rest of the oncological community of doctors and researchers viewed "cancer as a metabolic disease" (rather than as a genetic disease), we would (rather efficiently) conquer cancer with the same triumphant glory that we landed a man on the moon.

My copy of the book (get a copy here) is nearly all marked up. In addition to the compelling scientific analysis of cancer as a metabolic disease, what jumps off the page is the intensity of a brilliant, passionate scientist who has dedicated his life to challenging the entrenched paradigm with rigorous science and an equally sharp wit.

We'll barely scratch the surface of the wisdom in this great book (of course), but I'm excited to share some of my favorite paradigm-busting Big Ideas so let's jump straight in!

INCREASING ENTROPY

"It is important to recognize that prolonged reliance on substrate-level phosphorylation for energy production in previously normal respiring cells produces genome instability, disorder, and increased proliferation, that is, the hallmarks of cancer. Entropy refers to the degree of disorder in systems and is the foundation of the second law of thermodynamics. Szent-Gyorgi described cancer as a state of increased entropy, where randomness and disorder predominate. Protracted OxPhos insufficiency coupled with persistent compensatory fermentation increases entropy. Cells that do not increase fermentation energy to compensate for insufficient OxPhos simply die off and never become neoplastic. Adaptation to fermentation allows a cell to bypass mitochondrial-induced senescence. Cancer arises in those cells that bypass mitochondrial-induced senescence."

" If Warburg's views on the origins of cancer were correct then much of what is currently being done to manage the disease makes little sense. It is therefore important to carefully consider the evidence that irreversible respiratory injury is the origin of cancer."

~ Thomas Seyfried

That's from Chapter 4 in which we explore the "Energetics of Normal Cells and Cancer Cells." Again, this treatise is like a textbook. Seyfried walks us through the details of energy metabolism, etc. Here's what we need to know.

To establish cancer as a metabolic disease, we need to establish the fact that energy metabolism breaks down BEFORE the genomic instability sets in. And, that's what Professor Seyfried painstakingly does throughout the book.

He also helps resolve what's known as the "oncogenic paradox"—so named by Albert Szent-Gyorgi, a leading cancer researcher of his day. We talk about that in more detail in our Note on the journal article.

" It is my opinion that many cancer researchers, through their propensity to focus on gene mutations and mechanisms of action, have made the quest for cancer management far more complicated than it actually is."

~ Thomas Seyfried

Short story there: The "oncogenic paradox" is the fact that cancer can be initiated by a bunch of different things: radiation, chemicals, a virus, inflammation, etc. It's a really tough thing to explain when you view cancer as a genetic disease.

But, Seyfried walks us through how the paradox can be resolved when you step back and look at it from a metabolic perspective. What all those "provocative agents" have in common is the ability to create "respiratory insufficiency"—aka dysfunctional energy metabolism.

Seyfried also walks us through the "hallmarks of cancer" (uncontrolled growth, evasion of normal cell death, etc.) and connects THOSE to dysfunctional energy metabolism.

Again, for our oversimplified purposes: When your energy metabolism gets weird (technical term!), everything gets weird. Including your genome stability.

In short: Cause: Metabolic dysfunction. Effect: Genetic dysfunction.

P.S. We talked about Albert Szent-Gyorgyi in a prior Note. In fact, Eric Butterworth juxtaposes "entropy" with "syntropy" and puts it this way in *Spiritual Economics*: *"It is interesting to note that there is mounting evidence for the existence of ... 'syntropy,' through the influence of which forms tend to reach higher and higher levels of organization, order, and dynamic harmony. Albert Szent-Gyorgyi, Nobel Prize winning biologist, refers to it as an 'innate drive in living matter to perfect itself.' And today many are calling attention to a psychological drive toward synthesis, toward wholeness and self-perfection."*

I like it. Exit entropy. Enter syntropy. (All that's required? Optimize our energy metabolism. :)

NUCLEAR-CYTOPLASM TRANSFER STUDIES

" There are simply too many inconsistencies with the hypothesis that most cancers arise specifically from gene or chromosomal defects. The most damming evidence against the gene theory comes from the nucleus/cytoplasmic transfer experiments. ... Just because the majority of cancer researchers do not question the theory that guides their work does not mean that the theory is correct. Indeed, it appears that the average cancer researcher is not guided by any grand theory, rather they formulate restricted hypotheses for the next few experiments and tend to go on collecting data without reference to the problem of carcinogenesis."

~ Thomas Seyfried

"If all cancer arises from mitochondrial dysfunction, then replacement of damaged mitochondria with normal mitochondria should prevent cancer. In other words, mitochondria producing sufficient respiration should suppress tumor growth regardless of the numbers and types of mutations or aneuploidy present. ...

Further support for the Warburg theory would come from evidence showing that normal mitochondria can suppress malignant growth in tumor cells. If respiratory insufficiency is the origin of cancer, then tumor nuclei should not induce malignancy when placed in cytoplasm containing respiration competent normal mitochondria. Alternatively, if mitochondrial dysfunction is the origin of cancer, normal nuclei should be unable to prevent tumorigenesis when placed into the tumor cytoplasm. I refer to these types of experiments as *nuclear-cytoplasm transfer studies*. What is the evidence from these types of studies that support the metabolic origin of cancer?"

That's from Chapter 11: "Mitochondria: The Ultimate Tumor Suppressor" in which we review the REMARKABLE studies that provide, perhaps, the most compelling evidence establishing cancer as a metabolic disease. We've talked about these studies a few times already—in *Tripping over the Truth*, the journal article and Conquering Cancer 102.

Here's the super-quick recap: Imagine a cancerous cell. Both the nucleus (which contains the genes) and the cytoplasm (with the energy-metabolizing mitochondria) are cancerous.

Now, take the cancerous nucleus out and drop it into an otherwise healthy cell—leaving the healthy cytoplasm with the cancerous nucleus. What happens?

Do the same thing with the cancerous cytoplasm. Take it out and drop it into an otherwise healthy cell so you've got a healthy nucleus and a cancerous cytoplasm. What happens?

The gene theory says that your genes (/the nucleus) drive cancer. Therefore, the cancerous nucleus should result in a cancerous cell. BUT THAT DOESN'T HAPPEN!!!

"Delivery of a tumor cell nucleus into a normal cell cytoplasm begets normal cells despite the persistence of tumor-associated genomic abnormalities."

~ Thomas Seyfried

What does happen? Well, the healthy cytoplasm will basically turn off the cancerous nucleus's defects: *"It is also well documented that nuclei from cancer cells can be reprogrammed to form normal tissues when transplanted into normal cytoplasm despite the continued presence of the tumor-associated genomic defects in the cells of the derived tissues."*

<— THAT'S NOT SUPPOSED TO HAPPEN. But it does.

What's most disturbing is the fact that YOU now know more about this than your oncologist.

<— THAT'S NOT SUPPOSED TO HAPPEN. But it does.

Ahem. Back to the study. So, our healthy cytoplasm can reprogram (!) a cancerous nucleus. But... The cancerous nucleus is helpless in the presence of a cancerous cytoplasm. THAT hybrid cell becomes cancerous. Why? Because cancer is a metabolic disease.

As Seyfried says (nearly pleading) a few times in the book: *"Hello! Is anyone listening?"*

In this context, he says: "In summary, the origin of carcinogenesis resides with the *mitochondria* in the cytoplasm, not with the *genome* in the nucleus. How is it possible that so many in the cancer field seem unaware of the evidence supporting this concept? How it is possible that so many in the cancer field have ignored these findings while embracing the flawed gene theory? Perhaps Payton Rous was correct when he mentioned *'the somatic mutation theory acts like a tranquilizer on those who believe in it.'* I attribute the absence of any real progress in the war on cancer over the last 40 years to the flawed concepts of the somatic mutation theory, and to the failure in recognizing mitochondrial dysfunction as a credible scientific explanation for the origin of the disease. The failure is an inexcusable tragedy ultimately responsible for the deaths of millions of cancer patients."

Seriously. How is it possible that nearly everyone in the cancer world—from the National Cancer Institute (those $5 billion come from you and me, btw) to our oncologists (who work for you and me, btw)—has ignored this and all the other data supporting cancer as a metabolic disease?

These strong words are worth rereading as we take control of our own health destiny (as CONQUERORS (!) not "patients" a la our Notes on *Radical Remission*), refuse (!) to be a statistic, and help shape the future of cancer care: *"The failure is an inexcusable tragedy ultimately responsible for the deaths of millions of cancer patients."*

"If cancer is primarily a disease of energy metabolism, then rational strategies for cancer management should be found in those therapies that specifically target tumor cell energy metabolism. These therapeutic strategies should be applicable for the majority of cancers regardless of tissue origin, as nearly all cancers suffer from the same underlying disorder, that is, damaged respiration with compensatory fermentation."

~ Thomas Seyfried

METASTASIS AND MR. MO BUILDING YOUR MOAT

"*Metastasis* is the general term used to describe the spread of cancer cells from the primary tumor to surrounding tissues and to distant organs and is the primary cause of cancer morbidity and mortality. It is estimated that metastasis is responsible for about 90% of cancer deaths. This estimate has not changed significantly in more than 50 years. Although systematic metastasis is responsible for 90% of cancer deaths, most research in cancer does not involve metastasis in the in vivo state. That about 1,500 people continue to die each day from cancer further attests to the failure in managing the disease once it spreads to other organs."

Metastasis. In Greek, it literally means "to change." In the oncological world, it's a change for the worse—when a localized cancer spreads to another part of the body.

Metastasis is responsible for 90% (!!!) of cancer deaths. Therefore, it's THE most important thing we need to address as we look at how to conquer cancer.

This is why your traditional oncologist is literally willing to go to war on your body/immune system. In their words: slashing (surgery), burning (radiation) and poisoning (chemo) you with toxic therapies to try to halt the spread because they know that once a cancer metastasizes, they're REALLY bad at stopping it.

Enter (I wince as I type this): FIFTEEN HUNDRED (!!!) deaths from cancer every.single.day.

" We used linear regression analysis to show that growth of experimental astrocytoma was directly related to the levels of circulating glucose levels. It is clear from the figure that the higher the glucose level, the faster the growth. As glucose levels fall, tumor size (weight) and growth falls. ....
In light of these findings, it is difficult to understand why some oncologists would encourage cancer patients to consume high calorie foods and drinks during their treatment. Glucose accelerates tumor growth!"

~ Thomas Seyfried

To put that number in perspective, as horrific as the recent Stoneman Douglas High School shooting was (I can't even imagine the pain of the families and community), and as inspiring as it is to see the next generation stepping up to change the world, nearly ONE HUNDRED TIMES more people are killed by cancer EVERY DAY. (Gah.)

Again, I'm deliberately repeating myself here: Those are the stats we see when cancer is viewed as a *genetic* disease. From this perspective, cancer is an infinitely complex disease and, although we've been promised miracle, targeted therapies that are just around the corner, I wouldn't bet on those coming any time soon and/or those stats changing any time soon.

And, again, we're not talking about abstract numbers (as big as they are). This is my brother. Your brother. Your sister. Your mother. Your best friend. We can do better. And we MUST.

How? The metabolic approach to cancer. When viewed from the metabolic perspective (echo!) it's damaged mitochondria and energy metabolism that's the issue.

So, what do we do? We REHABILITATE our mitochondria and our energy metabolism!!!

One oversimplified way to think of it: Imagine your favorite athlete. When they get hurt, what do they do? *Rehabilitate*. Now, if you have cancer, think of YOURSELF as an (Olympic!) athlete. You're injured. It's time to hit your rehabilitation with everything you've got.

Back to the primary point of this idea: metastasis. We need to build a "moat" around our cancer to make sure it doesn't metastasize. And, if the cancer already has metastatized, we need to work *even* harder (like an OLYMPIC athlete!) to stop the growth and push it back.

Here's another oversimplified way to look at it: We need Mr. Mo to build our MOAT.

Mr. Mo? Yah. Mr. Mo. "Mr." "Mo" = "Mitochondrial Rehabilitation" + "Metabolic Optimization."

Mr. Mo builds our "MOAT" that makes sure cancer stays put (and goes kaput): Our "MOAT" = "My Oncologically Awesome Terrain." <— Remember Nasha Winter's genius statement: *"We need to treat the TERRAIN not the tumor."*)

All of which begs the question: *How* does Mr. Mo build our MOAT?

Enter: All the metabolically-oriented protocols we've been talking about in these Notes—from Nasha's *Metabolic Approach to Cancer*, Seyfried's journal articles, *Keto for Cancer*, *Outside the Box Cancer Therapies*, etc.

" In contrast to most conventional cancer therapies that expose both normal cells and tumor cells to toxic assaults, dietary restriction and particularly the KD-R [restricted ketogenic diet], are the only known therapies that can target tumor cells while enhancing the health and vitality of normal cells. In this regard, the KD-R as a cancer therapy is conceptually superior to many current conventional cancer therapies."

~ Thomas Seyfried

CELL DEATH: TWO TYPES: APOPTOTIC VS. NECROTIC

"Apoptotic cell death differs from necrotic cell death, which is usually associated with inflammation. Apoptotic tumor cell death would therefore be less provocative to the tumor microenvironment than would necrotic cell death, as tissue inflammation is less during apoptosis than during necrosis. This is important since the current standard of care for many cancers often involve radiation therapy together with toxic chemotherapy that causes inflammation and necrotic tumor cell death... In contrast to most conventional cancer therapies, which cause tissue necrosis and inflammation, metabolic therapies involving reduced calorie intake primarily kill tumor cells through apoptotic cell death. *Is it better to kill tumor cells using toxic drugs, as is currently done in the oncology field, or is it better to kill tumor cells using a nontoxic metabolic therapy like DER [dietary energy reduction]?* I favor the latter approach."

Did you know cells can die in one of two ways?

Apoptotic vs. Necrotic. One is natural and nontoxic. The other is unnatural and toxic. Which do you think is the wiser way to conquer cancer? You guessed it. Apoptotic.

How do we create apoptotic cell death? You guessed it. Approach cancer as a metabolic disease.

Specifically, a key component: *"Tumor cells have difficulty growing once their access to glucose*

and glutamine becomes limited. Indeed, Yuneva considers the dependence of tumor cells on glucose and glutamine for survival as the 'Achilles heel' of cancer. I concur with Dr. Yuneva's general assessment." <— See Miriam Kalamian's *Keto for Cancer* (Seyfreid wrote the foreword).

THE SUN IN THE CANCER SOLAR SYSTEM

"I have presented substantial evidence showing that respiratory damage underlies the origin of cancer. Cancer is a disease of energy metabolism. If respiratory injury is the prime cause of cancer then protecting mitochondria and respiration from damage becomes the prime means of preventing cancer."

~ Thomas Seyfried

"It is important to recognize that my view of cancer as a metabolic disease is not part of the mainstream view of cancer, which is viewed as an incomprehensively complex genetic disease. Support for my position comes from a perusal of the articles in the *Science* issue commemorating the anniversary of the US National Cancer Act. No aspect of cancer metabolism was mentioned in this issue. As mentioned in Chapter 10, *the failure to discuss the role of energy metabolism in the origin of cancer would be like failing to discuss the role of the sun in the origin of the solar system*. Should we be surprised that the same questions remain unresolved after 40 years? Should we be surprised that most targeted therapies developed from the cancer genome projects have been a costly waste of time? Should we be surprised that so little progress has been made in managing advanced cancers?"

Those are the last words of the book before Seyfried quickly recaps 18 "major conclusions." These are some strong words: *"the failure to discuss the role of energy metabolism in the origin of cancer would be like failing to discuss the role of the sun in the origin of the solar system."*

Now, even if you don't TOTALLY buy into the idea that cancer might be a metabolic disease, you'd think that an issue of *Science* magazine commemorating the War on Cancer would at least *mention* the fact that one of the primary differences between healthy and cancerous cells is their energy metabolism, right? Alas, no.

Which is another reason why we need to step up and be the CEOs of our health care as we push to conquer cancer. Sending love and let's do this.

Brian Johnson

If you liked this Note, you'll probably like…

- The Metabolic Approach to Cancer
- Keto for Cancer
- Tripping over the Truth
- Outside the Box Cancer Therapies
- Radical Remission
- Anticancer

About the Author of "Cancer as a Metabolic Disease"

THOMAS SEYFRIED

Dr. Seyfried published a groundbreaking treatise entitled, *Cancer as a Metabolic Disease: On the Origin, Management, and Prevention of Cancer* (Wiley, 1st ed., 2012). The treatise provides extensive information showing that cancer can be best defined as a mitochondrial metabolic disease rather than as a genetic disease. This new concept has implications for the development of new non-toxic cancer therapies including the ketogenic diet. Experts in the cancer research field have praised this comprehensive study as one of science's hottest topics.

About the Author of This Note

BRIAN JOHNSON

Brian Johnson loves helping people optimize their lives as he studies, embodies and teaches the fundamentals of optimal living—integrating ancient wisdom + modern science + common sense + virtue + mastery + fun. Learn more and optimize your life at optimize.me.