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Keto Staves Off Deadly Glioblastoma

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STORY AT-A-GLANCE -

- World renowned cancer biologist Thomas Seyfried recently published another case study demonstrating the power of a ketogenic diet to dramatically slow the progression of an invasive, fast-growing and usually deadly brain cancer, glioblastoma
- The mean survival with glioblastoma has not changed significantly in more than 100 years; Seyfried believes by drastically reducing the fermentation of glucose and glutamine — essential for cancer cell growth — you can improve overall survival
- Experts have advanced the theory that cancer is primarily the result of defective energy metabolism and not genetic mutation; this would have a significant impact on approaches to preventing, treating and managing cancer
- Seyfried's take home message is that you can help prevent cancer by maintaining healthy mitochondrial respiration. Consider using cyclical nutritional ketosis, calorie restriction, meal timing and exercise

Cancer is a disease of uncontrolled growth of abnormal cells. In 1971,[1] President Richard Nixon declared war on cancer with a goal to make a national commitment to find a cure. Chemotherapy has been one of the primary treatments used in cancer with the objective to destroy cancer cells.[2]

However, chemo is technically a poison. When administered it travels throughout your body and affects every cell, unlike radiation or surgical treatments, which target precise locations.[3]

Glioblastoma is a specific type of brain cancer that develops from glial cells in the brain.[4] It is sometimes referred to as a grade 4 astrocytoma. The tumor is fast-growing, invasive and commonly spreads throughout the brain. According to the Glioblastoma Foundation[5] it can result in death as quickly as 15 months after diagnosis.

Symptoms of a glioblastoma develop rapidly as the cells grow and fluid around the tumor increases pressure in the brain.[6] Some common symptoms include severe headaches, nausea and vomiting. Depending on the location of the tumor, symptoms can include weakness or sensory changes in the face, arms or legs, neurocognitive or memory issues and difficulty with balance.

Despite decades of research, researchers have written that the survival rate for individuals with glioblastoma multiforme (GBM) has not changed in more than 40 years.[7] Thomas Seyfried, who I believe is one of the best cancer biologists in the world, recently published an 80-month case report follow-up on a patient with glioblastoma,[8] who has lived far longer than expected.

Long-Term Care With Ketogenic Metabolic Therapy

Writing in the journal Nutrition & Metabolism in 2007,[9] Seyfried and colleagues proposed that restricting calories on a ketogenic diet is an effective alternative means of treating malignant brain cancer. The researchers used an animal model to test the theory and found the method was safe and effective.

August 16, 2014, a 26-year-old man presented at University Hospital Plymouth with symptoms of a malignant brain tumor.[10] The man refused the recommended standard of care and opted instead to use ketogenic metabolic therapy (KMT). He educated himself on the implementation of the diet despite pressure from health care professionals to use their treatment.

He took medication to control the seizures and strictly followed the **ketogenic diet**, monitoring his glucose and ketones. It took two weeks to enter therapeutic ketosis. A second MRI in January 2015 showed no noticeable progression of the tumor. Serial

MRIs every three to five months showed the tumor was growing slowly, quite unlike the natural progression of a glioblastoma.

Just over two years later, an MRI showed enough tumor growth that the patient decided to undergo a debulking surgery. Histological analysis showed an invasive astrocytic tumor. The tumor cells had a chance mutation known as IDH1, which improves the length of survival.[11] After surgery, the patient continued the ketogenic diet, maintaining his glucose ketone index (GKI) near or below 2.0.[12]

In October 2018, an MRI showed interval progression after the patient had relaxed his strict adherence to the ketogenic diet. He returned to eating a keto diet that kept his GKI at 2 and included additional interventions such as breathing exercises, stress management and moderate physical training.

Over the following 2.5 years and seven MRIs, the tumor showed slow interval progression. As of the time of the case study writing in April 2021, the patient was "active with a good quality of life, except for occasional tonic-clonic seizures and no signs of increased intracranial pressure."[13]

This case study is similar to one presented in 2018[14] of a 38-year-old man with a diagnosis of GBM. In addition to using a calorie-restricted ketogenic diet, this patient also underwent a subtotal tumor resection and used a modified standard of care treatment including epigallocatechin gallate, **hyperbaric oxygen therapy**, metformin and methylfolate.

After nine months of treatment, biomarkers and clinical symptoms indicated the tumor was regressing. At the time of the case study, 24 months after the start of therapy, the patient was in excellent health and showed evidence of significant tumor regression.[15]

Importance of Glucose and Glutamine to Cancer Cells

Seyfried commented in a press release from Boston College:[16]

> *"We were surprised to discover that KMT could work synergistically with the IDH1 mutation to simultaneously target the two major metabolic pathways needed to drive the growth of GBM. Glucose drives the glycolysis pathway, while glutamine drives the glutaminolysis pathway.*
>
> *No tumor, including GBM, can survive without glucose and glutamine. Our study has identified a novel mechanism by which an acquired somatic mutation acts synergistically with a low carbohydrate, high fat diet to provide long-term management of a deadly brain tumor."*

The team postulated that the long-term survival of the first patient whose follow-up case study was written at 80 months after diagnosis may have been in part due to the IDH1 mutation[17] and KMT, both targeting glycolysis and glutaminolysis essential for GBM growth.[18]

Glutamine is an amino acid that plays a role in intestinal health. Glucose and glutamine are fermentable fuels in the body. Studies[19] have suggested microbial protein fermentation plays a role in generating a range of molecules that may increase inflammation and tissue permeability.

Seyfried writes that glucose and glutamine may drive breast cancer growth "through substrate level phosphorylation (SLP) in both the cytoplasm (**Warburg effect**) and the mitochondria (Q-effect), respectively."[20]

In an interview with me, Seyfried describes how cancer cell metabolism is different from normal cell metabolism, changing from respiration to fermentation.[21] If you measure oxygen consumption in tumor cells it looks like they are using oxygen to make ATP. However, the mitochondria are abnormal and what Seyfried realized was that the cells were fermenting amino acids, and in particular glutamine.

Using an animal model,[22] Seyfried and colleagues demonstrated that with a calorically restricted ketogenic diet and a glutamine antagonist, they could reverse disease symptoms and improve animal survival. The strategy also appeared to reduce inflammation, swelling and hemorrhaging.

He also suggests that KMT with glutamine targeting may be an effective means of improving overall survival for women with breast cancer.[23] This means targeting **glucose and glutamine** in the treatment of cancer all but eliminates their source of energy and starves the cells, so they can't survive.

Why Cancer Is a Metabolic Disease

Western medicine has been operating under the theory that cancer is a genetic disease. This rules everything from research funding and treatment to the entire cancer industry. Unfortunately, despite decades of relying on this dogma, it has not led to any significant breakthrough in treatment or prevention.

Seyfried and others have advanced the theory that cancer is primarily the result of defective energy metabolism in, and damage to, the cell's mitochondria. Genetic mutations that are detectable in cancer cells are not the primary cause of cellular overgrowth but are rather a downstream effect of defective energy metabolism.[24]

Research data demonstrate that cancer growth is suppressed when the nucleus from a tumor cell is transferred to the cytoplasm of normal cells with normal functioning mitochondria.[25] This tells us that normal mitochondria can suppress cancer growth. Conversely, for cancer cells to proliferate, you must have dysfunctional mitochondria.

Seyfried's research has demonstrated the growth and progression of cancer can be managed using a "whole body transition from fermentable metabolites, such as glucose and glutamine, to respiratory metabolites."[26] These are primarily ketone bodies that are formed when you follow a ketogenic diet.

In "**Why Cancer Needs To Be Treated as a Metabolic Disease**," I discuss many of the pathways Seyfried notes in his interview with Dr. Peter Attia. Seyfried answers questions about the different types of mitochondrial abnormalities that are found in cancer cells and why cancer cells do not self-destruct.

Changing the view of cancer from a genetic disorder to primarily a metabolic disease has a significant impact on the approaches to preventing, treating and managing

cancer.[27]

Healthy Mitochondria Help Prevent Cancer

Seyfried's take-home message is that as long as your mitochondrial respiration remains healthy, cancer will not develop. There are several strategies you can use to help keep your mitochondria healthy. Avoiding toxic environmental factors and implementing healthy lifestyle strategies are the primary means of protecting your mitochondria.

In fact, this is the sole focus of the metabolic mitochondrial therapy program detailed in my book "Fat for Fuel." Topping my list of strategies to optimize mitochondrial health, which you can read more about in my book, are:

Cyclical nutritional ketosis — The divergence from our ancestral diet — this massive prevalence of processed, unnatural foods and excessive amounts of added sugars, net carbs and industrial fats — is responsible for most of the damage to your mitochondria.

Calorie restriction — Another extremely effective strategy for reducing mitochondrial free radical production is to limit the amount of fuel you feed your body. This is a noncontroversial position as calorie restriction has consistently shown many therapeutic benefits.

Meal timing **—** Meal timing is also important. Specifically, eating too late in the evening, when your body doesn't need the energy, is one of the worst things you can do to your mitochondria, as it creates a buildup of ATP that is not being used.

Normalizing your iron level — Iron also plays an important role in mitochondrial function, and contrary to popular belief, excessive iron levels are far more prevalent than iron deficiency. Virtually all men over the age of 16 and post-menopausal women are at risk of high iron.

Exercise — Exercise upregulates genes that promote mitochondrial efficiency,

helping them grow and divide so that you have more mitochondria. By placing an increased energy demand on your cells, free radicals signal that you need more mitochondria to meet the energy demand. As a result, your body adapts to your level of activity by creating more mitochondria and making them work more efficiently.

Nutritional supplements — The following nutrients and cofactors are also needed for mitochondrial enzymes to function properly:

- CoQ10 or ubiquinol (the reduced form)
- L-Carnitine, which shuttles fatty acids to the mitochondria
- D-ribose, which is raw material for the ATP molecule
- Magnesium
- Marine-based omega-3
- All B vitamins, including riboflavin, thiamine and B6
- Alpha-lipoic acid (ALA)

Sources and References

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