# Glioblastoma Alternative Cancer Treatment

**Research Report** 

# Brain Cancer Alternative Treatment

Written by Keith D. Bishop, C.N., B.Sc. Pharmacy Bishop Natural Cancer Reports

<u>www.NaturalCancerReports.com</u>

#### Introduction

I felt I shouldn't wait until I'm finished writing to share this FREE Glioblastoma Brain Cancer Alternative Treatment Report.

You need this information now and can start implementing the supplements listed in a couple of days.

This is a work in progress and has not been proofed by my editor. Please excuse the grammar and spelling mistakes. I'm sure my Okie accent comes through at times!

Please check back every few days to see if I have uploaded a newer version. Take a note of the version (upload date) at the bottom of the pages. I'll place the version on the web page next to the link.

Wishing you the best,

Keith

#### *Why I have Glioblastoma Brain Cancer Alternative Treatment Tips in each section.*

- I've been in health care since 1977, and a clinical nutritionist since 1998. In that time I've learned an enormous amount of information. When appropriate I want to share some of this knowledge for the general public. Since each person, cancer and medication is unique I can provide only general information rather than specific recommendations.
- I also provide links to supplements I use in my practice. I've selected supplement companies that provide effective, outstanding quality, cGMP products. You may click on the link to go to an information page to learn more about the supplement.
- 3. I do make a commission on the supplements if you purchase them through my registration page. This allows me to concentrate on writing this lifesaving information rather than running a retail store.

I've spent hundreds (yes hundreds) of hours researching and writing this "FREE" report. (I didn't work this hard when I was in pharmacy school!) When you purchase an item you are supporting my effort in providing <u>FREE information to</u> <u>you and others</u> in desperate need of improved outcomes.

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I do appreciate your support!

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Dietary supplements are not intended to diagnosis, treat, cure or prevent any disease.

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# Caffeine

In a large European population study researchers found coffee and tea consumption decreased the risk of glioblastoma.<sup>1</sup>

In glioblastoma laboratory cell cultures caffeine inhibited IP(3)R3mediated Ca(2+) release and inhibited migration (metastasis). Caffeine greatly increased survival times in mice with glioblastoma transplanted tumors.<sup>2</sup>

Treatment of glioblastoma cells with caffeine in a laboratory test demonstrated that caffeine caused the cancer cells to pause in the early S phase of cell division and growth.<sup>3</sup>

Caffeine is one of the most potent activators of an antioxidant repair system called Nrf2. Inhibiting Nrf2

enhanced the effectiveness of temozolomide (TMZ) chemotherapy. <sup>4</sup>

#### *Glioblastoma Brain Cancer Alternative Treatment Tip:*

**SPECIAL NOTE:** If you are taking Temodar (temozolomide / TMZ) and other chemotherapy drugs I would **NOT** consume <u>high</u> amounts of caffeine except tea.

Unless you have caffeine sensitivity, brew and drink organic strong coffee, up to espresso strength, four times daily, two cups in the morning, one after lunch and one midafternoon. If you are caffeine sensitive and have sleep problems consume 2-3 cups of strong coffee in the morning only. Coffee contains more caffeine than tea.

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<sup>&</sup>lt;sup>1</sup> Am J Clin Nutr. 2010 Nov;92(5):1145-50. Coffee and tea intake and risk of brain tumors in the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort study.

Michaud DS, Gallo V, et. al. Department of Epidemiology and Public Health, Imperial College, London, United Kingdom.

<sup>&</sup>lt;sup>2</sup> Cancer Res. 2010 Feb 1;70(3):1173-83.Caffeinemediated inhibition of calcium release channel inositol 1,4,5-trisphosphate receptor subtype 3 blocks glioblastoma invasion and extends survival. Kang SS, Han KS, et al.

<sup>&</sup>lt;sup>3</sup> Cell Cycle. 2008 May 15;7(10):1440-8DNA replication in early S phase pauses near newly activated origins. Frum RA, Chastain PD 2nd, et al, Department of Pathology and Laboratory Medicine, School of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina 27599-7525, USA.

<sup>&</sup>lt;sup>4</sup> Oncol Rep. 2013 Jan;29(1):394-400. Knockdown of Nrf2 enhances autophagy induced by temozolomide in U251 human glioma cell line. Zhou Y, Wang HD, Zhu L, et. al., Department of Neurosurgery, Jinling Hospital, School of Medicine, Nanjing University, Nanjing 210002, P.R. China.

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# CLA (Conjugated linoleic acid)

In a GBM laboratory cell study CLA strongly inhibited cell growth and proliferation rate and induced normal cell death (apoptosis). The CLA treatment decreased tumor cell migration and invasiveness via PPARgamma activation. Researchers state, "*this natural fatty acid (CLA) may be used as brain antitumor drug and as a chemopreventive agent.*" <sup>5</sup>

CLA inhibited GBM cell growth in cell studies. CLA was more effective against the more aggressive malignant cells. The inhibitory effect of CLA on growth was accompanied by programmed cell death and necrosis. The effects of CLA involved PPARs.

Researchers state: "In conclusion, CLA may be regarded as a component of the diet that exerts antineoplastic activity it effect may be antiproliferative or proapoptotic." <sup>6</sup> There have not been any animal or human CLA GBM studies.

There have not been any studies showing concerns about CLA and Glioblastoma.

#### *Glioblastoma Brain Cancer Alternative Treatment Tip:*

In my practice I use Xymogen ConjuLean 1000. Click here to learn more about ConjuLean 1000.

<sup>&</sup>lt;sup>5</sup> Int J Cancer. 2005 Dec 20;117(6):923-33. PPARgammadependent effects of conjugated linoleic acid on the human glioblastoma cell line (ADF). <u>Cimini A, Cristiano L, Colafarina</u> <u>S, Benedetti E, Di Loreto S, Festuccia C, Amicarelli F, Canuto RA, Cerù MP</u>. Department of Basic and Applied Biology, University of L'Aquila, L'Aquila, Italy. <u>cimini@univaq.it</u>

<sup>&</sup>lt;sup>6</sup> Int J Cancer. 2004 Dec 20;112(6):909-19. An overview of the effect of linoleic and conjugated-linoleic acids on the growth of several human tumor cell lines. <u>Maggiora M, Bologna M, Cerù MP, Possati L, Angelucci A, Cimini A, Miglietta A, Bozzo F, Margiotta C, Muzio G, Canuto RA.</u> Dipartimento di Medicina e Oncologia Sperimentale, Università di Torino, Torino, Italy.

# **Curcumin / Turmeric**

Curcumin has been verified as an anti-cancer compound via multiple molecular targets. Its effective mechanisms include cell cycle arrest (cell copying itself), inducing normal cell death (apoptosis), suppressing oncogenes (cancer growth genes), and enhancing tumor suppressor genes. In this study the efficacy of curcumin was testing in DBTRG cells in a laboratory setting. Curcumin exhibits superior cytotoxicity (cell toxicity) on glioblastoma in a dose and time dependent manner.

#### This is for the physicians:

Curcumin enhances p53 and p21 pathways, suppressed cdc2, inhibits RB pathway, suppresses phosphorylated RB, and suppresses Bax and caspases 3. Researchers stated: "*Curcumin appears to be an effective anti-glioblastoma drug through inhibition of the two core signaling pathways and promotion of the apoptotic pathway*."<sup>7</sup>

Researchers at Université du Québec à Montréal- Hôpital Sainte-Justine, in Montréal, Canada state, "Among the natural products shown to possess chemopreventive and anticancer properties,

curcumin is one of the most *potent.*" They investigated the effects of this natural product on the growth of human glioma U-87 cell that were transplanted into mice. Curcumin exerted significant anti-tumor effects on subcutaneous (just under the skin) and intracerebral (in the brain) gliomas. Curcumin slowed tumor growth rate and increased animal survival time. The mechanisms of the anti-tumor effects were partly related to the inhibition of angiogenesis (growth of new blood vessels to the tumor).8

Researchers at Department of Neurosurgery, Institute of Molecular Medicine and Genetics, Medical College of Georgia, Augusta, Georgia studied the effect of curcumin in human (T98G, U87MG, and T67) and rat (C6) glioma cell lines. They found curcumin sensitized glioma cells to chemotherapy agents cisplatin, etoposide, camptothecin and doxorubicin and radiation. The researchers state, "These findings support a role for curcumin as an adjunct to traditional chemotherapy and radiation in the treatment of brain cancer."9

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<sup>&</sup>lt;sup>7</sup> Int J Mol Med. 2010 Aug;26(2):217-24. The anti-cancer efficacy of curcumin scrutinized through core signaling pathways in glioblastoma.<u>Su CC</u>, <u>Wang MJ</u>, <u>Chiu TL</u>. Division of General Surgery, Buddhist Tzu Chi General Hospital, Hualien 97004, Taiwan, R.O.C.

<sup>&</sup>lt;sup>8</sup> <u>Mol Nutr Food Res.</u> 2010 Aug;54(8):1192-201. Curcumin inhibits tumor growth and angiogenesis in glioblastoma xenografts. <u>Perry MC</u>, <u>Demeule M</u>, <u>Régina A</u>, <u>Moumdjian R</u>, <u>Béliveau R</u>. Laboratoire de médecine moléculaire, Université du Québec à Montréal-Hôpital Sainte-Justine, Montréal, Canada. <u>perry.marie-claude@courrier.ugam.ca</u> <sup>9</sup> <u>J Neurochem</u>. 2007 Jul;102(2):522-38. Curcumin suppresses growth and chemoresistance of human

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Curcumin inhibits glioblastoma brain cancer cell growth via many cellular mechanisms.<sup>10</sup> <sup>11</sup> <sup>12</sup>

At the time of publication, curcumin's anti-cancer effect for <u>all</u> cancers has been published in over 1,330 medical research articles.

There have been limited animal studies. There have not been any human studies. There are not any studies showing concerns or failure of response.

Even though curcumin is not well absorbed when taken orally researchers believe it should be

glioblastoma cells via AP-1 and NFkappaB transcription factors. <u>Dhandapani KM, Mahesh VB, Brann DW</u>. Department of Neurosurgery, Institute of Molecular Medicine and Genetics, Medical College of Georgia, Augusta, Georgia 30912, USA. kdhandapani@mcg.edu

<sup>11</sup> <u>Neurosci Lett.</u> 2006 Oct 16;407(1):53-8. Curcumin activated both receptor-mediated and mitochondriamediated proteolytic pathways for apoptosis in human glioblastoma T98G cells. <u>Karmakar S, Banik NL, Patel SJ,</u> <u>Ray SK</u>. Department of Neurosciences, Medical University of South Carolina, 96 Jonathan Lucas Street, Suite 323K, P.O. Box 250606, Charleston, SC 29425, USA.

<sup>12</sup> Brain Tumor Pathol. 2005;22(2):79-87. Expression of the constitutively activated RelA/NF-kappaB in human astrocytic tumors and the in vitro implication in the regulation of urokinase-type plasminogen activator, migration, and invasion. <u>Tsunoda K, Kitange G, Anda T, Shabani HK, Kaminogo M, Shibata S, Nagata I</u>. Department of Neurosurgery, Nagasaki University School of Medicine, 1-7-1 Sakamoto-machi, Nagasaki 852-8501, Japan.

ktsuno@net.nagasaki-u.ac.jp

used in phase II and phase III human cancer studies.<sup>13</sup>

Researchers in India demonstrated that taking piperine with curcumin increased brain levels of curcumin.<sup>14</sup>

Earlier research demonstrates that taking piperine with curcumin can increase human curcumin levels by up to 2,000%.<sup>15</sup>

#### *Glioblastoma Brain Cancer Alternative Treatment Tip:*

Do not be alarmed if you notice dark yellow to orange urine while taking curcumin and piperine. This is evidence that piperine is increasing your blood levels of curcumin and eliminating curcumin through the kidneys. During cancer treatment I would allow the urine to remain dark, but not cloudy, to ensure high blood levels.

<sup>&</sup>lt;sup>10</sup> <u>Neurochem Res.</u> 2007 Dec;32(12):2103-13. Curcumin suppressed anti-apoptotic signals and activated cysteine proteases for apoptosis in human malignant glioblastoma U87MG cells. <u>Karmakar S, Banik NL, Ray SK</u>. Department of Neurosciences, Medical University of South Carolina, Charleston, SC 29425, USA.

<sup>&</sup>lt;sup>13</sup> <u>Arch Pharm (Weinheim).</u> 2010 Aug 19. Curcumin in Cancer Chemoprevention: Molecular Targets, Pharmacokinetics, Bioavailability, and Clinical Trials. <u>Shehzad A, Wahid F, Lee YS</u>. School of Life Sciences and Biotechnology, College of Natural Sciences, Kyungpook National University, Taegu, Korea.

<sup>&</sup>lt;sup>14</sup> Indian J Med Res. 2010 May;131:692-5. Adult attention deficit/hyperactivity disorder: one year follow up. <u>Sitholey P</u>, <u>Agarwal V</u>, <u>Tripathi A</u>. Department of Psychiatry, C.S.M. Medical University, Lucknow, India.

<sup>&</sup>lt;sup>15</sup> <u>Planta Med.</u> 1998 May;64(4):353-6. Influence of piperine on the pharmacokinetics of curcumin in animals and human volunteers. <u>Shoba G, Joy D, Joseph T, Majeed M,</u> <u>Rajendran R, Srinivas PS</u>. Department of Pharmacology, St. John's Medical College, Bangalore, India.

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The dark urine and cloudiness may create some confusion when a lab or doctor does a UA (urinalysis). If you are scheduled to do a UA you may want to avoid curcumin with Bioperine for 24 hours prior to the UA.

Piperine / Bioperine has not been studied with GBM.

Additional piperine / Bioperine information is available at <u>http://www.bioperine.com/curcumi</u> <u>n.html</u>

In my practice I use CurcuPlex CR. Click here to learn more about CurcuPlex Cr.

#### EGCG (epigallocatechin-3gallate)

The Department of Neurosciences, Medical University of South Carolina, Charleston, SC, induced apoptosis (normal cell death) in human glioblastoma T98G and U87MG laboratory cells after treatment (-)-epigallocatechin-3gallate (EGCG). Their results strongly suggest that flavonoids are potential therapeutic agents for induction of apoptosis in human glioblastoma cells.<sup>16</sup>

Researchers in Germany treated three glioblastoma cell lines (U87, A172 and U251) with EGCG. EGCG treatment down regulated tumor cell growth via PEA15 and Akt (PKB) mechanisms.<sup>17</sup>

Canadian researchers found EGCG down regulated glioblastoma cancer cell growth via multiple MMP-mediated cellular events.<sup>18</sup>

<sup>17</sup> <u>Neurosci Lett.</u> 2008 Dec 19;448(1):161-5. Epigalocatechin-3-gallate (EGCG) downregulates PEA15 and thereby augments TRAIL-mediated apoptosis in malignant glioma. <u>Siegelin MD, Habel A, Gaiser T</u>. Department of Neuropathology, University Hospital Heidelberg, Im Neuenheimer Feld 220, 69120 Heidelberg, Germany. <u>markus.siegelin@med.uni-heidelberg.de</u> Low doses of EGCG induced apoptosis (normal cell death) and in glioblastoma cell lines U-373 MG, U-87 MG and C6. IFG-1 may be involved in the effects of EGCG.<sup>19</sup>

There have not been any human GBM studies with EGCG. There have not been any animal GBM studies with EGCG.

There have not been any failures of response with EGCG glioblastoma cancer studies.

#### *Glioblastoma Brain Cancer Alternative Treatment Tip:*

<u>I use GreenTea 600 in my practice.</u> <u>Click here to learn more about</u> <u>GreenTea 600.</u>

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<sup>&</sup>lt;sup>16</sup> <u>Cancer.</u> 2010 Jan 1;116(1):164-76. Flavonoids activated caspases for apoptosis in human glioblastoma T98G and U87MG cells but not in human normal astrocytes. <u>Das A,</u> <u>Banik NL, Ray SK</u>. Department of Neurosciences, Medical University of South Carolina, Charleston, SC 29209, USA. <u>swapan.ray@uscmed.sc.edu</u>

<sup>&</sup>lt;sup>18</sup> Biochim Biophys Acta. 2002 Jan 30;1542(1-3):209-20. Green tea polyphenol (-)-epigallocatechin 3-gallate inhibits MMP-2 secretion and MT1-MMP-driven migration in glioblastoma cells. <u>Annabi B, Lachambre MP, Bousquet-Gagnon N, Page M, Gingras D, Beliveau R</u>. Centre de Cancérologie Charles-Bruneau, Hôpital Ste-Justine et

Université du Québec à Montréal, C.P. 8888, Succ. Centreville, H3C 3P8, Montreal, QC, Canada. <sup>19</sup> <u>Neuro Oncol.</u> 2001 Jan;3(1):22-8. Inhibitory effect of epigallocatechin-gallate on brain tumor cell lines in vitro. <u>Yokoyama S, Hirano H, Wakimaru N, Sarker KP, Kuratsu J</u>. Department of Neurosurgery, Faculty of Medicine, Kagoshima University, Japan.

#### **Fermented Wheat Germ Extract** (FWGE) (OncoMar - AveMar)

FWGE has not been studied in GBM but has shown promising effects in lymphoma<sup>20</sup>, melanoma<sup>21</sup>, leukemia<sup>22</sup> <sup>23</sup>, colorectal cancer<sup>24</sup> <sup>25</sup>

<sup>26</sup>, breast cancer<sup>27</sup> and pancreatic cancer<sup>28</sup> studies.

FWGE works in several mechanisms including decreased energy production and use of glucose in cancer cells.<sup>29 30</sup>

GBM growth is stimulated by glucose and elevated blood glucose levels. Patients with normal blood glucose levels live longer than those with elevated blood glucose

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Institute, Torrance, California 90502, USA.

boros@gcrc.humc.edu

<sup>&</sup>lt;sup>20</sup> Oncol Rep. 2009 Mar;21(3):787-91. Avemar, a nontoxic fermented wheat germ extract, attenuates the growth of sensitive and 5-FdUrd/Ara-C cross-resistant H9 human lymphoma cells through induction of apoptosis. Saiko P, Ozsvar-Kozma M, Graser G, Lackner A, Grusch M, Madlener S, Krupitza G, Jaeger W, Hidvegi M, Agarwal RP, Fritzer-Szekeres M, Szekeres T. Clinical Institute of Medical and Chemical Laboratory Diagnostics, Medical University of Vienna, General Hospital of Vienna, A-1090 Vienna, Austria. <sup>21</sup> Cancer Biother Radiopharm. 2008 Aug;23(4):477-82. Adjuvant fermented wheat germ extract (Avemar) nutraceutical improves survival of high-risk skin melanoma

patients: a randomized, pilot, phase II clinical study with a 7year follow-up. Demidov LV, Manziuk LV, Kharkevitch GY, Pirogova NA, Artamonova EV. Melanoma Unit, Department of General Surgery, N.N. Blokhin Cancer Research Center, Russian Academy of Medical Sciences, Moscow, Russian Federation. info@eso.ru

Cancer Lett. 2007 Jun 8;250(2):323-8. Avemar, a nontoxic fermented wheat germ extract, induces apoptosis and inhibits ribonucleotide reductase in human HL-60 promyelocytic leukemia cells. Saiko P, Ozsvar-Kozma M, Madlener S, Bernhaus A, Lackner A, Grusch M, Horvath Z, Krupitza G, Jaeger W, Ammer K, Fritzer-Szekeres M, Szekeres T.

Clinical Institute of Medical and Chemical Laboratory Diagnostics, Medical University of Vienna, General Hospital of Vienna, Waehringer Guertel 18-20, A-1090 Vienna, Austria

<sup>&</sup>lt;sup>23</sup> J Biol Chem. 2002 Nov 29;277(48):46408-14. Epub 2002 Sep 25. Fermented wheat germ extract inhibits glycolysis/pentose cycle enzymes and induces apoptosis through poly(ADP-ribose) polymerase activation in Jurkat Tcell leukemia tumor cells. <u>Comin-Anduix B, Boros LG, Marin</u> <u>S, Boren J, Callol-Massot C, Centelles JJ, Torres JL, Agell</u> <u>N, Bassilian S, Cascante M</u>. Department of Biochemistry and Molecular Biology, CeRQT-PCB at Barcelona Scientific Park, University of Barcelona, 1 Marti i Franquès, Barcelona 08028, Spain.

<sup>&</sup>lt;sup>24</sup> Orv Hetil. 2005 Sep 11;146(37):1925-31. [Fermented wheat germ extract in the supportive therapy of colorectal cancer] Farkas E. Biromedicina Elso Magyar Rákkutatási Részvénytársaság, Budapest.

elek.farkas@biromedicina.com <sup>25</sup> Carcinogenesis.</u> 2001 Oct;22(10):1649-52. Wheat germ extract inhibits experimental colon carcinogenesis in F-344 rats. Zalatnai A, Lapis K, Szende B, Rásó E, Telekes A, Resetár A, Hidvégi M. 1st Institute of Pathology and

Experimental Cancer Research, Semmelweis University, Budapest, Hungary. zalatnai@korb1.sote.hu <sup>26</sup> Hepatogastroenterology. 2000 Mar-Apr;47(32):393-5. First clinical data of a natural immunomodulator in colorectal cancer. Jakab F, Mayer A, Hoffmann A, Hidvégi M. Department of Surgery, Uzsoki Teaching Hospital, Budapest, Hungary. Cancer Biother Radiopharm. 2004 Dec;19(6):746-53. The efficacy of tamoxifen in estrogen receptor-positive breast cancer cells is enhanced by a medical nutriment. Marcsek Z, Kocsis Z, Jakab M, Szende B, Tompa A. National Institute of Chemical Safety, "József Fodor" National Center for Public Health, Budapest, Hungary. marcsekz.okbi@okk.antsz.hu <sup>28</sup> Pancreas. 2001 Aug;23(2):141-7. Wheat germ extract decreases glucose uptake and RNA ribose formation but increases fatty acid synthesis in MIA pancreatic adenocarcinoma cells. Boros LG, Lapis K, Szende B, Tömösközi-Farkas R, Balogh A, Boren J, Marin S, Cascante M, Hidvégi M. UCLA School of Medicine, Harbor-UCLA Research and Education Institute, Torrance, California 90502, USA. boros@gcrc.humc.edu <sup>29</sup> J Biol Chem. 2002 Nov 29;277(48):46408-14. Epub 2002 Sep 25. Fermented wheat germ extract inhibits glycolysis/pentose cycle enzymes and induces apoptosis through poly(ADP-ribose) polymerase activation in Jurkat Tcell leukemia tumor cells. Comin-Anduix B, Boros LG, Marin <u>S, Boren J, Callol-Massot C, Centelles JJ, Torres JL, Agell</u> <u>N, Bassilian S, Cascante M</u>. Department of Biochemistry and Molecular Biology, CeRQT-PCB at Barcelona Scientific Park, University of Barcelona, 1 Marti i Franquès, Barcelona 08028, Spain. <sup>30</sup> Pancreas. 2001 Aug;23(2):141-7. Wheat germ extract decreases glucose uptake and RNA ribose formation but increases fatty acid synthesis in MIA pancreatic adenocarcinoma cells. Boros LG, Lapis K, Szende B, Tömösközi-Farkas R, Balogh A, Boren J, Marin S, Cascante M, Hidvégi M. UCLA School of Medicine, Harbor-UCLA Research and Education

levels.<sup>31 32 33 34</sup> Limiting the glucose metabolism with diet and FWGE may have beneficial effects.

There are no cell, animal or human fermented wheat germ extract GBM studies.

#### *Glioblastoma Brain Cancer Alternative Treatment Tip:*

<u>I use OncoMAR - AveMAR in my</u> <u>clinical nutrition practice. Click here</u> <u>to learn more about OncoMAR /</u> <u>AveMAR.</u>

<sup>&</sup>lt;sup>31</sup> <u>ASN Neuro.</u> 2010 Jul 23;2(3):e00038. Calorie restriction as an anti-invasive therapy for malignant brain cancer in the VM mouse. <u>Shelton LM, Huysentruyt LC, Mukherjee P, Seyfried</u> <u>TN</u>. Boston College, Higgins Hall, 140 Commonwealth Avenue, Chestnut Hill, MA 02467, U.S.A. <u>ASN Neuro.</u> 2010 Jul 23;2(3):e00038.

<sup>&</sup>lt;sup>32</sup> <u>Cell Cycle.</u> 2010 Jul 15;9(14):2742-8. microRNA-451: A conditional switch controlling glioma cell proliferation and migration. <u>Godlewski J, Bronisz A, Nowicki MO, Chiocca EA, Lawler S</u>. Dardinger Laboratory for Neuro-oncology and Neurosciences, The Ohio State University Medical Center and James Comprehensive Cancer Center, Columbus, OH, USA.

<sup>&</sup>lt;sup>33</sup> J Clin Oncol. 2009 Mar 1;27(7):1082-6. Epub 2009 Jan 12. Association between hyperglycemia and survival in patients with newly diagnosed glioblastoma. <u>Derr RL, Ye X, Islas MU,</u> <u>Desideri S, Saudek CD, Grossman SA</u>. c/o The NABTT CNS Consortium, Cancer Research Building #2, Suite 1M-16, 1550 Orleans St, Baltimore, MD 21231, USA. rderr@jhmi.edu

<sup>&</sup>lt;sup>34</sup> <u>Neurosurgery</u>. 2008 Aug;63(2):286-91; discussion 291. Persistent outpatient hyperglycemia is independently associated with decreased survival after primary resection of malignant brain astrocytomas. <u>McGirt MJ, Chaichana KL, Gathinji M, Attenello F, Than K, Ruiz AJ, Olivi A, Quiñones-<u>Hinojosa A</u>. Department of Neurosurgery, Johns Hopkins School of Medicine, and The Johns Hopkins Neuro-oncology Surgical Outcomes Research Laboratory, Baltimore, Maryland, USA</u>

#### Genistein

The Medical University of South Carolina found genistein triggered oxidative damage that induced normal cell death (apoptosis) in human glioblastoma cell lines T98G and U87MG.<sup>35</sup>

German researchers found genistein targets genes involved in the progression of the M-phase of the cell cycle.<sup>36</sup>

The College of Pharmacy and Biomedical Research Institute, at Idaho State University, found that genistein induced a decrease in invasive activity of U87MG glioblastoma cells in a dose-related manner. The higher the dose the better the genistein worked.

Genistein also induced a decrease in EGF-stimulated (epidermal growth factor) invasion thereby implicating an involvement of EGFmediated signaling in invasion.<sup>37</sup> Researchers at the University of Vermont, College of Medicine cultured and grew glioblastoma cells from three different glioblastoma patients. Genistein inhibited spreading of cancer cells in two of the three glioblastoma cancer cell lines.<sup>38</sup>

Researchers at University Hospital Utrecht, The Netherlands discovered that genistein inhibited both epidermal growth factor (EGF) and platelet-derived growth factor (PDGF) stimulated autophosphorylation of the receptors and induction of DNA synthesis. Genistein seemed to physically damage the cancer cells.<sup>39</sup>

There are no genistein animal glioblastoma studies. There are no genistein human glioblastoma studies. There have not been any failures in response to genistein.

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<sup>&</sup>lt;sup>35</sup> Cancer. 2010 Jan 1;116(1):164-76. Flavonoids activated caspases for apoptosis in human glioblastoma T98G and U87MG cells but not in human normal astrocytes. Das A, Banik NL, Ray SK. Department of Neurosciences, Medical University of South Carolina, Charleston, SC 29209, USA. <sup>36</sup> BMC Med Genomics. 2008 Oct 10;1:49. The molecular basis of genistein-induced mitotic arrest and exit of self-renewal in embryonal carcinoma and primary cancer cell lines. Regenbrecht CR, Jung M, Lehrach H, Adjaye J.Max Planck Institute for Molecular Genetics, Department for Vertebrate Genomics, Ihnestr, 73, D-14195 Berlin, Germany. <sup>37</sup> ] Neurooncol. 2006 Sep;79(2):135-42. Inhibition of matrix degrading enzymes and invasion in human glioblastoma (U87MG) cells by isoflavones. Puli S, Lai JC, Bhushan A. Department of Pharmaceutical

Sciences, College of Pharmacy and Biomedical Research Institute, Idaho State University, Pocatello, ID 83209, USA.

<sup>&</sup>lt;sup>38</sup> Neurosurgery. 1997 Jan;40(1):141-51. Inhibition of epidermal growth factor receptor-associated tyrosine kinase blocks glioblastoma invasion of the brain. Penar PL, <u>Khoshyomn S</u>, <u>Bhushan A</u>, <u>Tritton TR</u>. Division of Neurosurgery, University of Vermont College of Medicine, Burlington, USA.

<sup>&</sup>lt;sup>39</sup> <u>Neurosurgery.</u> 1996 Jan;38(1):108-13; discussion 113-4. Inhibitors of protein tyrosine phosphorylation reduce the proliferation of two human glioma cell lines. <u>Oude Weernink</u> <u>PA, Verheul E, Kerkhof E, van Veelen CW, Rijksen G.</u> Laboratory for Medical Enzymology, University Hospital Utrecht, The Netherlands.

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# Quercetin

Laboratory studies found quercetin effectively blocked migration and invasion of U87 glioblastoma cells while inhibiting COX-2/PGE(2) production, MMP-9 enzyme activity and peroxide production. Researchers believe quercetin possesses the potential to be developed for use against migration and invasion by glioblastomas.<sup>40</sup>

Three natural flavonol compounds were studied for their anti-cancer effect. Quercetin was found to be the most potent against U251 human glioblastoma cells.<sup>41</sup>

There are no human glioblastoma studies with quercetin. There are no animal glioblastoma studies with quercetin. There are no failures tumor responses to quercetin.

#### *Glioblastoma Alternative Brain Cancer Treatment Tip:*

In my practice I use Resveratin Plus for source of Quercetin. Click here to learn more about Resveratin.

<sup>&</sup>lt;sup>40</sup> Neurobiol Dis. 2010 Jan;37(1):118-29. Contribution of reactive oxygen species to migration/invasion of human glioblastoma cells U87 via ERK-dependent COX-2/PGE(2) activation. <u>Chiu WT</u>, <u>Shen SC</u>, <u>Chow JM</u>, <u>Lin CW</u>, <u>Shia LT</u>, <u>Chen YC</u>. Department of Neurosurgery, Taipei Medical University-Shuang Ho Hospital, Taipei, Taiwan. <sup>41</sup> <u>Z Naturforsch C</u>. 2002 Nov-Dec;57(11-12):1092-5. Flavonols from Scurrula ferruginea Danser (Loranthaceae). <u>Lohézic-Le Dévéhat F, Tomasi S, Fontanel D, Boustie J</u>. Laboratoire de Pharmacognosie et de Mycologie, UPRES 2234, Rennes Cedex. <u>Iohezic.francoise@libertysurf.fr</u>

#### Resveratrol

Resveratrol treatment of human glioblastoma cells induces a delay in cell cycle progression during S phase. This slows cancer cell growth by interfering with cells dividing and making copies of themselves. <sup>42 43</sup>

Research in Italy found resveratrol inhibited glioblastoma invasiveness by decreasing MMP-2 mRNA and SPARC gene and protein levels.<sup>44</sup>

Pterostilbene (PS), a natural dimethylated analogue of resveratrol, is known to have diverse pharmacologic activities including anticancer, antiinflammation, antioxidant, apoptosis, antiproliferation, and analgesic potential.<sup>45</sup> Resveratrol and pterostilbene have not been studied in animal nor human glioblastomas. There have not been any studies showing failure of response on glioblastoma cells.

#### *Glioblastoma Brain Cancer Alternative Treatment Tip:*

I use Resveratin Plus in my clinical nutrition practice for my source of resveratrol. Click here to learn more about Resveratin.

<sup>&</sup>lt;sup>42</sup> <u>Cancer Lett.</u> 2010 Sep 28;295(2):167-72. Resveratrol induces DNA double-strand breaks through human topoisomerase II interaction. <u>Leone S, Cornetta T, Basso E,</u> <u>Cozzi R</u>. Dipartimento di Biologia, Università degli Studi Roma Tre, Roma, Italy.

<sup>&</sup>lt;sup>43</sup> <u>Mol Carcinog.</u> 2008 Aug;47(8):587-98. Resveratrol and X rays affect gap junction intercellular communications in human glioblastoma cells. <u>Leone S, Fiore M, Lauro MG,</u> <u>Pino S, Cornetta T, Cozzi R</u>. Dipartimento di Biologia, Università Roma TRE, Rome, Italy.

<sup>&</sup>lt;sup>44</sup> <u>Biomed Pharmacother.</u> 2005 Aug;59(7):359-64. Effect of resveratrol on matrix metalloproteinase-2 (MMP-2) and Secreted Protein Acidic and Rich in Cysteine (SPARC) on human cultured glioblastoma cells. <u>Gagliano N, Moscheni C,</u> <u>Torri C, Magnani I, Bertelli AA, Gioia M</u>. Department of Human Morphology, University of Milan, Via Fratelli Cervi 93, 20090 LITA Segrate, Milan, Italy. <u>nicoletta.gagliano@unimi.it</u>

<sup>&</sup>lt;sup>45</sup> J Agric Food Chem. 2010 Aug 11;58(15):8833-41. Pterostilbene inhibits colorectal aberrant crypt foci (ACF) and colon carcinogenesis via suppression of multiple signal transduction pathways in azoxymethane-treated mice. <u>Chiou</u> <u>YS, Tsai ML, Wang YJ, Cheng AC, Lai WM, Badmaev V, Ho</u> <u>CT, Pan MH</u>. Department of Seafood Science, National Kaohsiung Marine University, Kaohsiung 811, Taiwan

#### Sulforaphane

Researchers at the Medical University of South Carolina treated human glioblastoma T98G and U87MG cells with sulforaphane. The sulforaphane caused GBM to commit apoptosis (normal cell death) via multiple cellular mechanisms.<sup>46</sup>

Since sulforaphane is relatively new, there has been limited research on Glioblastoma Brain Cancer.

Sulforaphane does not have human GBM studies. This does not mean it doesn't work. It's just too new.

#### *Glioblastoma Brain Cancer Alternative Treatment Tip:*

Sulforaphane increases glutathione levels in the body. According the theory sulforaphane may interfere with glioblastoma radiation and chemotherapy treatment.

#### To be on the safe side... *I currently do NOT recommend sulforaphane during radiation and some chemotherapy*

<u>treatments, including</u> <u>temozolomide (Temodar/TMZ),</u> <u>unless specifically stated in a</u> <u>particular Natural Cancer</u> <u>chemotherapy drug Report.</u>

I use <u>Nrf2 Activator</u>, <u>OncoPLEX ES</u>, and <u>I5 Protein Powder</u> for my sources of Sulforaphane.

<sup>&</sup>lt;sup>46</sup> <u>Neuroscience.</u> 2006 Sep 1;141(3):1265-80. Activation of multiple molecular mechanisms for apoptosis in human malignant glioblastoma T98G and U87MG cells treated with sulforaphane. <u>Karmakar S, Weinberg MS, Banik NL, Patel</u> <u>SJ, Ray SK</u>. Department of Neurosciences, Medical University of South Carolina, 96 Jonathan Lucas Street, Suite 323K, P.O. Box 250606, Charleston, SC 29425, USA.

#### **Alternative Cancer Treatment Consultations**

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