The Deadly Link

CANCER
INSULIN  GLUCOSE  OBESITY

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Research and Education

Integrative Women's Health Summit
October 2016  London UK
Integrative Cancer Care: Increased Rates of Cancer & Cancer Mortality Associated with Obesity & Insulin Resistance

Nutraceutical & Botanical Interventions

CREATE AN ENVIRONMENT WHERE CANCER CANNOT THRIVE

National Association of Nutrition Professionals Conference 2016
Is There a Connecting Link between Obesity, Diabetes and Cancer? Yes!!!!

Obesity is the strongest link between cancer and diabetes.
Obesity May Account for 14% of All Cancer Deaths in Men and 20% in Women

1 in 11 adults have diabetes (415 million)

46.5% of adults with diabetes are undiagnosed
UK
It is estimated that more than one in 16 people in the UK has diabetes (diagnosed or undiagnosed)\(^2\).
There are 4 million people living with diabetes in the UK.

UNDIAGNOSED
It is estimated that there are around 549,000 people in the UK who have diabetes but have not been diagnosed\(^7\).
DIAGNOSED

Around 700 people a day are diagnosed with diabetes. That’s the equivalent of one person every two minutes\(^3\).

Since 1996, the number of people diagnosed with diabetes in the UK has more than doubled from 1.4 million to almost 3.5 million\(^4\).

Today, there are almost 3.5 million\(^5\) people who have been diagnosed with diabetes in the UK (2014)\(^5\).

By 2025, it is estimated that five million people will have diabetes in the UK\(^6\).
March 10, 2016

according to a UCLA study

In California one third of young adults are at risk of becoming diabetic

Nearly half of California adults, including one out of every three young adults, have either pre-diabetes — a precursor to type 2 diabetes or undiagnosed diabetes

“This is the clearest indication to date that the diabetes epidemic is out of control and getting worse,” Dr. Harold Goldstein, executive director of the health advocacy center...
Diabetes around the world

Number of people (20-79 years) living with diabetes who are undiagnosed, 2015
Global Projections for the Diabetes Epidemic: 2003-2025

NA
23.0 M
36.2 M
\(\uparrow 57.0\%\)

EUR
49.4 M
58.6 M
\(\uparrow 21\%\)

EMME
19.2 M
39.4 M
\(\uparrow 105\%\)

SEA
39.3 M
81.6 M
\(\uparrow 108\%\)

AFR
7.1 M
15.0 M
\(\uparrow 111\%\)

WP
43.0 M
75.8 M
\(\uparrow 79\%\)

World
2003 = 194 M
2025 = 333 M
\(\uparrow 72\%\)

M = million, AFR = Africa, NA = North America, EUR = Europe, SACA = South and Central America, EMME = Eastern Mediterranean and Middle East, SEA = South-East Asia, WP = Western Pacific.

Does diabetes increase mortality in cancer?

Meta-analysis suggests that diabetes is associated with an increased mortality compared with normoglycemic individuals across all cancer types [hazard ratio (HR) 1.41 (95% CI 1.28–1.55)] particularly in patients with cancers of the endometrium, breast and colorectum.

Insulin Resistance and Cancer Risk: An Overview of the Pathogenetic Mechanisms

- Insulin resistance
- Adiponectin
- Inflammation
- Gluconeogenesis
- Hyperglycaemia
- Hyperinsulinemia
- ROS
- Mitosis
- DNA damage
- Anti-apoptosis
- Migration
- Angiogenesis

Genetic susceptibility
Environmental factors
Obesity

↑ FFA
↑ TG
↑ TNF-α
↑ IL-6
↑ Gluconeogenesis
↑ IGF-1
↑ IGFBPs
↑ Estradiol
↑ ROS
↑ IGF-I, estradiol and testosterone bioactivity
↑ Leptin
↑ PAI-1
↑ VEGF

Exp Diabetes Res. 2012; Biagio Arcidiacono, et al
Which Cancers Are Associated With Diabetes?

**Increased Risk:**

- Pancreatic
- Gastric
- Esophageal
- **Colorectal**
- Liver
- Gall Bladder
- Breast
- Ovarian

**Uncertain Link**

- Lung Cancer

**Endometrial**

- Cervical
- Urinary Bladder
- Renal
- Multiple Myeloma
- Non-Hodgkins
- Lymphoma

**Conflicting Studies**

- Prostate
Pre-operative diagnosis of diabetes appears to increase risk of post-operative mortality for some cancers.

In a meta-analysis of 15 reported studies, pre-existing diabetes was associated with increased odds of postoperative mortality across all cancer types, when controlled for confounders and publication bias [odds ratio (OR) = 1.51 (1.13–2.02)], compared with their non-diabetic patients undergoing operative treatment for cancer.

Poorer Outcomes

There is evidence that poor glycemic control can lead to **poorer outcomes in cancer therapy**.

Amongst patients with poorly controlled diabetes (HbA1c > 7.5%), a significantly 
**increased incidence of right-sided polyps** ($P = 0.001$), a **greater number of polyps** ($P < 0.005$), **more advanced polyps** and ($P < 0.005$), and a 
**younger age of presentation** ($P = 0.001$) was noted.
Obesity

Research shows that reducing caloric intake lowers the risk of cancer.

"the most compelling scenario for cancer development may include a combination of prolonged obesity due to excess caloric intake plus the resulting increase of circulating insulin, IGF’s cytokines and inflammatory molecules."

DIABETES AND CANCER—
AN AACE/ACE CONSENSUS STATEMENT
Yehuda Handelsman, MD, et al
Obesity is a common risk factor for diabetes and cancer.

Cancers consistently associated with Obesity

- Breast
- Endometrial
- Pancreas
- Esophageal
- Renal Cell
- Colorectal
- Liver


The Warburg Effect

A switch to anaerobic glycolysis is an adaptive change characteristic of rapidly proliferating cells.

Most cancer cells, unlike normal cells, rely more on glycolysis than oxidative phosphorylation to meet their energy needs, even under normoxic conditions.

Importantly, because glycolysis is far less efficient at generating ATP, most cancer cells require higher levels of glucose than normal cells to proliferate and survive.

This is why the glucose analog, 18fluorodeoxyglucose, is capable of detecting the majority of human tumors via positron emission tomography (PET SCAN).
Cancer cells produce energy by taking up glucose at much higher rates & using a smaller fraction of the glucose for energy production. This allows cancer cells to function more like fetal cells, promoting extremely rapid growth.

Warburg Effect
Aerobic Glycolysis
The Warburg Effect

Glycolysis leads to the secretion of lactic acid, which can decrease the extracellular pH from 7.4 to 6.0 within a poorly perfused tumor.

Lactate Promotes Metastasis could significantly reduce metastasis by reducing tumor-associated angiogenesis, extracellular matrix degradation, and the inhibition.
Bowker, Samantha, Johnson, Jeffrey.

**Hyperglycemia and cancer**

2014 Aug 13; Diapedia 6104476154 rev. no. 15.

Available from:
http://dx.doi.org/10.14496/dia.6104476154.15
How Might Diabetes Cause Cancer?
Diabetes and Cancer: Two Diseases With Obesity As A Common Risk Factor.

Diabetes Obes Metab. 2014 Feb;16(2):97-110. Garg SK1, Maurer H, Reed K, Selagamsetty R.
Insulin Resistance

A pathological condition characterized by a decrease in efficiency of insulin signaling for blood sugar regulation.

Insulin resistance is a major component of metabolic syndrome, i.e. a group of risk factors that generally occur together and increase the risk for various diseases, Type 2 Diabetes Mellitus, Obesity, CVD and Cancer.
Insulin is a Growth Factor

Elevated levels of insulin have been shown to be a risk factor for a number of cancers.

Diabetes Obes Metab. 2014 Feb;16(2):97-110. Garg SK et al
Most, if not all, tumor cells have a high demand on glucose compared to benign cells of the same tissue and conduct glycolysis even in the presence of oxygen (the Warburg effect).

In addition, many cancer cells express insulin receptors (IRs) and show hyperactivation of the IGF1R-IR pathway.

Evidence exists that chronically elevated blood glucose, insulin and IGF1 levels facilitate tumorigenesis and worsen the outcome in cancer patients.
Lifestyle Factors
Poor Diet
Sedentarism

Insulin Resistance
HyperInsulinemia

Diabetes

Hyperglycemia

Co-Morbidities
Vascular Disease
Infection

Obesity

Inflammation

Cancer

Inflammation

Insulin IGF-1

Mortality

Diabetes Obes Metab. 2014 Feb;16(2):97-110. Garg SK et al
The Interactions of Obesity, Inflammation and Insulin Resistance in Breast Cancer

- Obese postmenopausal women have an increased breast cancer risk.
- The principal mechanism for which is elevated estrogen production by adipose tissue.
- Regardless of menstrual status and tumor estrogen dependence, obesity is associated with biologically aggressive breast cancers.
- Type 2 diabetes has a complex relationship with breast cancer risk and outcome.
- Coexisting obesity may be a major factor.
- Insulin itself induces adipose aromatase activity and estrogen production.
- And also directly stimulates breast cancer cell growth and invasion.

Inflammation & Cancer Survival

Survival of Cancer Patients Correlated to the Level of Inflammation

- LOW
- HIGH

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Omega-3 fatty acids reduce obesity-induced tumor progression

Obesity and inflammation are both risk factors for a variety of cancers, including breast cancer in postmenopausal women. Intake of omega-3 polyunsaturated fatty acids (ω-3 PUFAs) decreases the risk of breast cancer, and also reduces obesity-associated inflammation and insulin resistance,

OMEGA 3 Fatty Acids

EPA-DHA Triglyceride Form

2000-6000mg/day
Insulin Resistance and Breast Cancer

Insulin Resistance → Hyperinsulinemia

- Increased Aromatase
  - Increased Free Estrogen

- Reduced SHBG

- Increased IGF-BP
  - Increased Free IGF-1

Cancer

T.A.Chowdhury QJM 2010:103:905-15
Oxford Univ.Press
The Role of Dietary CHO Restriction in Cancer Development and Outcome
CHO Restriction
Ketogenic Diet

The involvement of the glucose-insulin axis may also explain the association of the metabolic syndrome with an increased risk for several cancers.

CHO restriction has already been shown to exert favorable effects in patients with the metabolic syndrome.

Epidemiological and anthropological studies indicate that restricting dietary CHO(s) could be beneficial in decreasing cancer risk.
Dietary CHO Restriction

- Low CHO diets cause a drop in plasma insulin and lactate
- Low CHO diets can reduce insulin-mediated glucose uptake into tumor cells
- Hyperglycemia Enhances Proliferation in some tumors
- Insulin is the primary growth factor and driver of proliferation (Insulin Makes Glucose Available)
- Tumor Size and Growth is Related to Plasma Insulin Levels and Plasma Lactate Levels
A low carbohydrate, high protein diet slows tumor growth and prevents cancer initiation.

Cancer cells rely more heavily on glycolysis than normal cells. 10% or 20% CHO High Protein diet slows tumor growth as effectively as No CHO Ketogenic Diets. Ketogenic Diets reduces BG, insulin, and glycolysis, slows tumor growth, reduces tumor incidence, and works additively with existing therapies.

Many cancer patients, those with advanced stages of the disease, exhibit altered whole-body metabolism marked by cachexia:

- increased plasma levels of inflammatory molecules
- impaired glycogen synthesis
- increased proteolysis in muscle tissue
- increased fat utilization in muscle tissue
- increased lipolysis in adipose tissue
- increased gluconeogenesis by the liver

- High fat, low CHO (Ketogenic) diets aim at these metabolic alterations
- High Fat low CHO diets are safe and likely beneficial, in particular for advanced stage cancer patients.
CHO Restriction

CHO & Calorie Restriction

Ketogenic Diet

• CHO restriction mimics the metabolic state of calorie restriction or - in the case of KDs - fasting.

• The beneficial effects of calorie restriction and fasting on cancer risk and progression are well established.

• CHO restriction thus opens the possibility to target the same underlying mechanisms without the side-effects of hunger and weight loss.
CHO Restriction
Ketogenic Diet

Some laboratory studies indicate a direct anti-tumor potential of ketone bodies. During the past years, a multitude of mouse studies indeed proved anti-tumor effects of KDs for various tumor types, and a few case reports and pre-clinical studies obtained promising results in cancer patients as well. Several registered clinical trials are going to investigate the case for a KD as a supportive therapeutic option in oncology.
Daily Therapeutic Ketogenic Shake
1-2 shakes per day

Make thick or thin according to your preference
May sip on each shake over several hours
Not necessary to consume all at once

Mix with choice of unsweetened coconut milk (best brands are free of carageenan), coconut water, green tea, filtered water

Take each shake with digestive enzymes
Protease Formula 2 caps with full shake  (take 1 cap with each 1/2 shake) *avoid Betaine Hydrochloride*

Lipase Concentrate 2 caps with full shake  (take 1 cap with each 1/2 shake)

If you are nauseous from the high fat content you can double the dose of the Lipase
Daily Therapeutic Ketogenic Shake  1-2 shakes per day
Protein Powder = 35-40 grams of protein per shake
Medium Chain Triglycerides 1 tablespoon
Carnitine Tartrate 1/2 teaspoon (1.5-2.0 g)
Phosphatidyl Choline  1 heaping teaspoon (170mg choline)
Phosphatidyl Serine 1/2 teaspoon (400mg)
Acetyl L Carnitine 1/2 teaspoon (1.5g)
Cordyceps, Coriolus, Ganoderma 3 grams each
Omega 3, 6, 7, 9 Essential Fatty Acids 1-2 TBS (4-6 g)
Concentrated reds and greens powders 2 tsp
Black Chia Seeds 1 tablespoon
Hemp Seeds 1 tablespoon
Fiber Powder (Soluble+Insoluble fibers) 1-2 heaping tsp.

Add 1/2 organic lemon with the peel
Optional: mint, orange zest, ginger, cinnamon, cardamom, vanilla, cacao nibs, fresh greens, spinach, parsley, kale
Low CHO
High Protein
High EFA
Ketogenic Shakes
Obesity
A Major Risk Factor
Obesity is Recognized a Major Risk Factor

Obesity is associated with worsened prognosis after cancer diagnosis and also negatively affects the delivery of systemic therapy, contributes to morbidity of cancer treatment, and may raise the risk of second malignancies and comorbidities.

Research shows that the time after a cancer diagnosis can serve as a teachable moment to motivate individuals to adopt risk-reducing behaviors.
American Society of Clinical Oncology
Position Statement on Obesity and Cancer

- Obesity can interfere with the effective delivery of systemic cancer therapy and can contribute to morbidity from treatment.

- Obesity is a risk factor for poor wound healing, postoperative infections, and lymphedema, as well as for the development of comorbid illness (eg, heart disease, cerebrovascular disease, and diabetes), in cancer survivors.

- Obesity also places individuals at increased risk of developing second primary malignancies.

JCO November 1, 2014 vol. 32 no. 31 3568-3574
• A recent meta-analysis of 82 studies including more than 200,000 patients with breast cancer demonstrated a 75% increase in mortality in premenopausal women and a 34% increase in mortality in postmenopausal women who were obese at the time of breast cancer diagnosis, as compared with patients who were of normal weight at diagnosis.7

• Obese men seem to be at increased risk of developing biologically aggressive prostate cancers and also are more likely to have advanced disease at the time of prostate cancer diagnosis.

• A BMI ≥ 35 kg/m2 may be associated with an increased risk of colon cancer recurrence and mortality

• Emerging data suggest that obesity may be a prognostic factor in other malignancies
How Does Obesity Increase Cancer Risk?

Insulin Resistance and Cancer Risk: An Overview of the Pathogenetic Mechanisms

Exp Diabetes Res. 2012; Biagio Arcidiacono, et al
Quantity and Diversity of Plant Foods
Whole Grains  Legumes
Raw & Cooked Vegetables
Fresh & Dried Fruits
Nuts  Olive Oil  Fish
Moderate Red Wine
Moderate Meat & Dairy
(goat/sheep)
Stepping it up a notch: Energy restriction diets

- Animal studies have shown protective effects of daily continuous energy restriction (CER) and weight loss on reducing tumor formation over 100 years of research.
- Clinical data that weight reduction reduces breast cancer risk (observational studies, one large RCT and bariatric surgery trials).
- However CER is difficult to maintain, thus intermittent energy restriction (IER) or intermittent fasting (IF) have been studied as strategies with greater potential for compliance.
  - Mirrors Paleolithic periods of food abundance and scarcity
  - Traditional Mediterranean diet includes periodic fasting
  - Continuum of energy restricted diets:
    - Overnight Fast $\geq 12$ hr
    - 2 days/week $< 500$ kcal/d
    - 10%-15% continuous caloric restriction
Energy Restricted Diets and IGF-1

- 6 months of IER (2 d/week of 70% ER) led to greater improvements in insulin sensitivity even on non-restricted days compared to an isoenergetic CER diet.
- A 23% decrease of insulin ($P = 0.001$) with a further 25% reduction in insulin on the restricted days.
- IGF-1 levels and IGF-1 activity are lower in IER animals compared to CER animals on isocaloric diets.
- Alternate days of fasting (IER) also reduce mammary cell proliferation by 30%.

Nutrients that Reduce the Proliferative Effect of Insulin and IGF-1

- Magnesium 300-600mg
- Chromium 300 mcg tid
- Berberine 500-2000mg
- Tocotrienols 1000mg bid
Berberine
Isoquinoline Alkaloid
found in roots and rhizomes of

• Scutellaria baicalensis (Huang Qin)
• Coptis Chinensis (Huang Lian)
• Phellodendron amurense (Huang Bai)
• Hydrastis canadensis (Goldenseal)
• Berberis aquifolium (Oregon Grape)
• Berberis vulgaris (Barberry)
A number of scientific studies have demonstrated the **Hypoglycemic Effects of Berberine on T2DM**

- Improves insulin sensitivity
- Promotes insulin secretion
- Regulates glucose and lipid metabolism in liver via modulating the PPARs protein expression
- Reduces intestinal absorption of glucose
- Antioxidant activity protective of diabetic complications
- Modulates the composition of gut microbiota (enrichment of beneficial microbiota and inhibition of harmful microbiota)

Berberine: Anti-Neoplastic Effects
Suppresses the growth of a wide variety of tumor cells, including

breast cancer, leukemia, melanoma, epidermoid carcinoma, hepatoma, pancreatic cancer, oral carcinoma, tongue carcinoma, glioblastoma, prostate carcinoma, gastric carcinoma.
Berberine: Anti-Neoplastic Effects

Inhibits
- Apoptosis
- Carcinogenesis
- Inflammation: NFkB, TNFa, IL6, COX2,
- Inhibits CAM (Cell Adhesion Molecules)
- (TNF-α, IL-6, COX-2, adhesion molecules, cyclin D1)
- Stress-induced mitogen-activated protein kinase activation. (MAPK)
- Multi Drug Resistance (MDR)

RadioSensitizer
Anti-Microbial
Effects of Berberine on Glucose Metabolism

Antioxidant & anti-inflammatory activities of berberine in the treatment of diabetes mellitus.

Application of berberine on treating type 2 diabetes mellitus.

Pang B, Zhao LH, Zhou Q, Zhao TY, Wang H, Gu CJ, Tong XL.
Nutrients to Reduce the Proliferative Effects of Insulin and IGF-1

- Magnesium
- Chromium

Glucose

- blood glucose
- CHO restriction
- Dietary restriction

IGF1R

IGF1

Insulin

IR

PI3K

Akt

mTOR

AMPK

PPAR

+ Berberine
+ Tocotrienols

↑ fatty acid oxidation
Mitochondrial biogenesis
↑ aerobic glycolysis (inhibits Warburg effect)
Antioxidants
Autophagy

Targeting Inflammation by Nutraceuticals in Obesity and Insulin Resistance

- Curcumin
- Capsaicin
- Polyunsaturated fatty acids
- Ginger-derived components
- Flavonoids
- Resveratrol and stilbenes

Myung-Sunny Kim, et al. N.Y. Acad. Sci. ISSN 0077-8923
ANNALS OF THE NEW YORK ACADEMY OF SCIENCES
Issue: Nutrition and Physical Activity in Aging, Obesity, and Cancer
Curcuminoids exert glucose-lowering effect in type 2 diabetes by decreasing serum free fatty acids: a double-blind, placebo-controlled trial.

Curcuminoids supplementation (300mg/d x 3 months) significantly decreased

- Fasting Blood Glucose (p < 0.01),
- HgbA1c (p = 0.031)
- Insulin Resistance Index (HOMA-IR) (p < 0.01)
- Serum Total FFAs (p < 0.01),
- Triglycerides (P = 0.018), an

Mol Nutr Food Res. 2013 Sep;57(9):1569-77.
Na LX, Li Y, Pan HZ, Zhou XL, Sun DJ, Meng M, Li XX, Sun CH.

F. Amin, et al. Clinical efficacy of the co-administration of Turmeric and Black seeds (Kalongi) in metabolic syndrome – A double blind randomized controlled trial – TAK-MetS trial, Complementary Therapies in Medicine, 2015, 23, 2, 165


Shatadal Ghosh, et al. The beneficial role of curcumin on inflammation, diabetes and neurodegenerative disease: A recent update, Food and Chemical Toxicology, 2015, 83, 111


Muralidhara Rao Maradana, Ranjeny Thomas, Brendan J. O'Sullivan, Targeted delivery of curcumin for treating type 2 diabetes, Molecular Nutrition & Food Research, 2013, 57, 9
Curcumin-induced alterations reverse insulin resistance, hyperglycemia, hyperlipidemia, and other symptoms linked to obesity.

Other structurally homologous nutraceuticals, derived from red chili, cinnamon, cloves, black pepper, and ginger, also exhibit effects against obesity and insulin resistance.
Curcumin directly interacts with pancreatic cells, hepatic stellate cells, macrophages, and more.

Suppresses the proinflammatory transcription factors nuclear factor-kappa B, signal transducer activators of transcription-3, Wnt/β-catenin

Activates peroxisome proliferator-activated receptor-γ (PPAR-γ) and Nrf2 cell-signaling pathways

Down-regulates adipokines, tumor necrosis factor, interleukin-6, resistin, leptin, and monocyte chemotactic protein-1

Upregulates adiponectin and other gene products
Modulation by curcumin of various targets linked to obesity. Orange/yellow boxes indicate downregulation, and blue boxes indicate upregulation.

Bharat Aggarwal
<table>
<thead>
<tr>
<th>Effect</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>↑ beta-cell function</td>
<td>Weisberg SP, Leibel R, Tortoriello DV. Endocrinology 2008;149:3549-3558.</td>
</tr>
<tr>
<td>↓ adipogenesis</td>
<td></td>
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<tr>
<td>↓ leptin → ↓ liver fibrosis in fatty liver</td>
<td></td>
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<tr>
<td>↓ inflammation in adipocytes</td>
<td></td>
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<tr>
<td>↑ insulin sensitivity</td>
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</table>
Targeting Inflammation-Induced Obesity and Metabolic Diseases by Curcumin and Other Nutraceuticals

Bharat B. Aggarwal

- Capsaicin Capsicum spp. fructus *Cayenne*
- Cinnamaldehyde Cinnamomum spp. cortex *Cinnamon*
- Gingerol Zingiber officinale rhizome *Ginger*
- Piperine Piper nigrum fructus *Black Pepper*
- Fenugreek Trigonella foenum-graecum semen

Significantly decreased
High-sensitivity C-reactive protein
(-26%, p = 0.03),
Tumor necrosis factor-α
(-19.8%, p = 0.01),
Plasminogen activator inhibitor type 1
(-16.8%, p = 0.03), and
Interleukin-6/interleukin-10 ratio
(-24%, p = 0.04)

Increased anti-inflammatory
Interleukin-10 (19.8%, p = 0.00) and
Adiponectin (6.5%, p = 0.07)
Green Tea Catechin EGCG and Resveratrol Stilbenes

Short-term supplementation with a specific combination of dietary polyphenols increases energy expenditure (EE) and alters substrate metabolism in overweight subjects.

We demonstrated for the first time that combined EGCG (282mg bid) + RESV (200mg bid) supplementation for 3 days significantly increased fasting and postprandial EE, which was accompanied by improved metabolic flexibility in men but not in women. Addition of soy isoflavones partially reversed these effects possibly due to their higher lipolytic potential. The present findings may imply that long-term supplementation of these dosages of epigallocatechin-gallate combined with resveratrol may improve metabolic health and body weight regulation.

Branched Chain Amino Acids Improve Insulin Resistance and prevent progressive liver failure

**Isoleucine** regulates blood sugar, formation of blood cells, supports muscle growth and repair.

**Valine** helps support the recovery and muscle building process and nervous system functioning.

**Leucine** direct regulator of the muscle-building pathways that activate the mTOR complex, turns on protein synthesis.
Green Tea Catechins

Branched Chain Amino Acids

Development of Obesity-related CRC


The diabetes epidemic is out of control and getting worse.

Chronically elevated blood glucose, insulin and IGF1 levels facilitate tumorigenesis and worsen the outcome in cancer patients.

Obesity is the strongest link between cancer and diabetes.
Lifestyle Factors
- Poor Diet
- Sedentarism

Diabetes
- Insulin Resistance
- Hyperinsulinemia
- Hyperglycemia
- Co-Morbidities
  - Vascular Disease
  - Infection

Obesity
- Inflammation
- Insulin IGF-1

Cancer

Mortality

Diabetes Obes Metab. 2014 Feb;16(2):97-110. Garg SK et al
## Cancers Associated With Increased Risk of Diabetes

<table>
<thead>
<tr>
<th>Increased Risk</th>
<th>Conflicting studies</th>
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</thead>
<tbody>
<tr>
<td>Pancreatic</td>
<td>Endometrial</td>
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<tr>
<td>Gastric</td>
<td>Cervical</td>
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<td>Esophageal</td>
<td>Urinary Bladder</td>
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<td>Lymphoma</td>
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<tr>
<td>Ovarian</td>
<td></td>
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<tr>
<td>Weak Link</td>
<td></td>
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<tr>
<td>Lung Cancer</td>
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Obesity is a common risk factor for diabetes and cancer.

Obesity is the strongest link between cancer and diabetes.

Cancers Associated With Obesity

- Breast
- Endometrial
- Pancreas
- Esophageal
- Renal Cell
- Liver
- Colorectal

Reducing caloric intake lowers the risk of cancer
Insulin Resistance and Breast Cancer

Insulin Resistance

Hyperinsulinemia

- Increased Free Estrogen
- Increased Aromatase
  - Reduced SHBG
  - Increased Free IGF-1

Cancer

Most cancer cells unlike normal cells rely more on glycolysis.

Cancer cells produce energy by taking up glucose at much higher rates & using a smaller fraction of the glucose for energy production...promoting extremely rapid growth.
A Low Carbohydrate High Protein Diet

• slows tumor growth
• prevents cancer initiation
• reduces blood glucose
• reduces insulin
• reduces glycolysis
• reduces tumor incidence
CANCER
INSULIN  GLUCOSE  OBESITY

Curcumin  Resveratrol
Green Tea Catechins  Flavonoids
Ginger  Capsaicin  Piperine
Cinnamon  Fenugreek
Berberine  Tocotrienols

Magnesium  Chromium
Polyunsaturated Fatty Acids
Branched Chain Amino Acids
Mediterranean Diet  Calorie Restriction
Ketogenic Diet  CHO Restricted Diet
Exercise
The Deadly Link

CANCER

INSULIN  GLUCOSE  OBESITY

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Founder, American Institute of Integrative Oncology
Research and Education

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Conference 2016