Cancer and Angiogenesis

Preliminaries

Some forty years ago a theory that a growing tumor could be “starved to death” by cutting off its blood supply was presented in the *New England Journal of Medicine*. It was met with skepticism, ridicule, and dismissal. This theory was called anti-angiogenesis. Today there are twelve anti-angiogenic drugs on the market for cancer treatment, with twenty-six more in the final stages of human testing, and another hundred-plus in human trials. Every major pharmaceutical company has an angiogenesis program, and the first FDA-approved anti-angiogenic cancer drug, Avastin, is becoming a household name.

The summary below is taken from the current work of Professor William Li and his research team. Anti-angiogenesis treatment for cancer is absolutely mainstream, cutting-edge treatment for cancer. It is not an alternative theory of medicine. It is not a theory cobbled together from research papers and theories, then presented in a mass market bestseller. Rather, William Li and his team work in oncology and are conducting much of the research themselves in their laboratories, universities, and clinics.

Introduction to Angiogenesis

Angiogenesis is the growth of new blood vessels. It is now well established that cancerous tumor growth is dependent upon angiogenesis. In virtually every healthy adult there are microscopic cancer cells, the result of errors during replication of 60–90 trillion cells. To gain sustenance to grow, these small microscopic clusters of 60–80 cells may migrate toward existing host blood vessels in order to obtain nutrients. Autopsy studies have shown that these microscopic cancers are present in the breasts of up to 40% of women between the ages of forty and fifty years, and in 50% of prostates in men between fifty and sixty years. By age seventy, microscopic
cancers are detected in the thyroids of virtually everyone. Most of these
tumors never become clinically significant, leading to the concept of
“cancer without disease” as a normal state during aging.

In normal healthy adults, angiogenesis (the growth of new blood
vessels) is suppressed except for brief bursts during the female
reproductive cycle, pregnancy, and wound healing. This means the
cancerous cells which are found within most people as they age do not
develop into a tumor because the cells are not able to obtain a supply of
nutrients from new blood vessel growth. However, in some cases, tumors
recruit new blood vessels from surrounding vessels, an event known as the
“switch” to the angiogenic phenotype. This enables them to grow and
spread, leading to cancer in the individual.

Anti-angiogenesis is therefore stopping the blood vessels from growing
or forming. Anti-angiogenic drug therapy consists of targeting the blood
vessels in order to cut off the supply of nutrients to the tumor. Without a
supply of nutrients the tumor shrinks and eventually disappears. This
form of cancer treatment has been validated as an effective cancer
treatment strategy for a growing number of cancer types, including
colorectal, renal, liver, lung, brain, pancreatic neuroendocrine tumors,
gastrointestinal stromal tumors, multiple myeloma, and myelodysplastic
syndrome. Moreover, anti-angiogenic drugs are now available for many
advanced malignancies including colorectal, lung, breast, kidney, liver,
brain, thyroid, neuroendocrine, multiple myeloma, and myelodysplastic
syndrome.

Using Anti-Angiogenic Treatment to Prevent Cancer

This is where things get interesting. Potent anti-angiogenic molecules have
now been identified in dietary sources. This suggests that an anti-
angiogenic diet could provide a safe, widely available, and novel strategy
for preventing cancer. In testing, numerous foods, such as strawberries
and green tea, outperformed anti-angiogenic drugs. These foods, which
are listed below, have been shown to prevent tumor growth, not through
any antioxidant effects, but because they are anti-angiogenic—they stop blood vessels feeding cancer cells.

This is not to give false hope to current cancer sufferers: anti-angiogenic drugs currently remain the best option for targeting cancerous tumors that have already formed. However, an anti-angiogenic diet that prevents new blood vessel growth would not be harmful and the current evidence suggests should help to cut off the blood supply to tumors. There is also growing evidence that glucose aids tumor growth. An anti-angiogenic diet and a diet which restricts glucose are not incompatible. Moreover, an anti-angiogenic diet is also good for preventing heart disease, inflammation, and age-related cognitive decline. It can be adjusted to accommodate the cuisine of just about every ethnicity or genetic phenotype. The macronutrients (fats, carbohydrates, and protein) ratios can also be adjusted according to need. Before outlining the diet a word or two about angiogenesis and obesity is necessary.

In tests on laboratory mice, genetically bred to be fat and then fed junk food, their weight can be controlled by giving them anti-angiogenic drugs. When given these drugs their weight drops dramatically to that of normal mice; when the drug is stopped their weight balloons. The theory behind this observation is that adipose tissue recruits new blood vessels; if this supply is disrupted through anti-angiogenesis then the adipose tissue shrinks. In laboratory tests this theory has been confirmed. The suggestion is that eating an anti-angiogenic diet will help to prevent cancer and heart disease, stave off cognitive decline, and help to reduce obesity.

Anti-Angiogenic Factors in Dietary Sources

There are a good number of confirmed, tested anti-angiogenic foods. The full list, which is still expanding, is at the end of this essay. There are, however, a number of foods that deserve special mention.
Green Tea Catechins

Clinical trials are underway in Western and Asian nations to study the chemo-preventive potential of green tea for oral, prostate, skin, and other cancers. Laboratory studies have demonstrated that green tea and its catechins prevent mutagenesis, cancer invasion and metastases, and angiogenesis. Polyphenol catechins in tea, predominantly flavanols, possess anti-angiogenic activity. Epigallocatechin-3-gallate (EGCG) is a potent tea flavonoid. Mice that consume 1.25% green tea (the human equivalent of drinking two to three cups of tea per day) show inhibition of VEGF-stimulated corneal neo-vascularization by as much as 70% and a reduction of tumor cell invasion by 50%. Polyphenon E, an extract from green tea leaves containing a defined mixture of polyphenolic catechins, is in clinical trials for prostate, bladder, esophageal, lung, head and neck cancers, and leukemia.

Resveratrol

Resveratrol inhibits angiogenesis in the chick CAM assay, suppresses VEGF- and bFGF-induced corneal neo-vascularization, and inhibits tumor vascularization in mice. Resveratrol also inhibits chemically induced mammary carcinogenesis, skin cancer tumorigenesis, and tumor growth and metastasis in mice. In mice with full thickness skin wounds, resveratrol delays wound healing angiogenesis and the time required for complete wound closure. A number of anti-angiogenic mechanisms have been identified.

Omega-3

Both preclinical and epidemiological studies suggest that omega-3 PUFAs are effective cancer preventative agents. Omega-3 PUFAs inhibit angiogenesis and may competitively inhibit the bioconversion of omega-6 PUFAs into their angiogenesis-promoting derivatives such as prostaglandins and arachidonic acid. In contrast, omega-6 PUFAs, present at high levels in sunflower oil, peanut oil, and corn oils, have been shown
in vitro to stimulate endothelial migration and tube formation. Intake of omega-3 PUFAs from seafood has been associated with a decreased risk for certain cancers, including pancreatic, colon, breast, and prostate cancer.

Menaquinone
A form of vitamin K, menaquinone (vitamin K2), found in certain food sources is anti-angiogenic and associated with a reduced risk for developing several forms of cancer. Menaquinone is distinct from the phylloquinone (vitamin K1) present in dark leafy vegetables. Instead, menaquinone is a fat soluble vitamin formed naturally by bacteria in fermented dairy products, including cheese and yogurt, in fermented soy such as natto, and also present in dark meat. Certain cheeses, such as Dutch Gouda, Swiss Emmental, and Norwegian Jarlsberg, have particularly high concentrations of menaquinone. In laboratory studies, menaquinones suppress angiogenesis, enhance tumor apoptosis, and inhibit the proliferation of cancer cells.

Curcumin
Curcumin has chemo-preventive and anti-angiogenic activity and inhibits carcinogenesis in skin, stomach, intestines, and liver. Dietary ingestion of curcumin has been shown to prevent the formation of colon polyps, suppress proliferation of colon cancer and prostate cancer cells, and decrease intratumoral microvessel density.

<table>
<thead>
<tr>
<th>List of Anti-Angiogenic Foods</th>
<th>Blackberries</th>
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<tbody>
<tr>
<td>Fruits</td>
<td>Blueberries</td>
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<td>Apples</td>
<td>Cherries</td>
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</tbody>
</table>
Clementines  Thyme
Cranberries  Turmeric
Grapefruit
Lemons
Nectarines
Oranges
Peaches
Pomegranates
Raspberries
Red grapes
Strawberries
Tomatoes

**Herbs & Spices**

Basil
Black pepper
Cilantro
Cinnamon
Cloves
Cocoa powder
Flaxseed
Garlic
Ginger
Ginseng
Lavender
Licorice root
Nutmeg
Oregano
Parsley
Rosemary
Tarragon
Thistle

**Vegetables**

Artichokes
Beets
Bok choy
Broccoli
Brussels sprouts
Cabbages (red, savoy, white)
Carrots
Cauliflower
Chard
Collard greens
Endives
Fennel
Garlic
Kale
Mustard greens
Olives
Onions
Peas
Parsnips
Peppers
Pumpkins
Radishes
Salsify
Scallions
Shallots
Soybean sprouts
Spinach
String beans
Sweet potatoes
Turnips and their tops
Watercress
Winter squashes (acorn, butternut)

**Oils, Sauces & Condiments**
Honey
Maple syrup
Olive oil
Soy sauce

**Mushrooms**
Enoki mushrooms
King oyster mushrooms
Maitake mushrooms
Matsutake mushrooms
Oyster mushrooms
Reishi mushrooms
Shiitake mushrooms

**Seafood**
Cuttlefish
Flounder
Haddock
Halibut
Herring
Mackerel
Oysters
Salmon
Sardines
Sea cucumbers
Seaweed (Arame, Dulse, Hijiki, Kombu, Mozuku, Nori Wakame)

**Meats**
Chicken (dark meat)
Goose (dark meat)
Turkey (dark meat)

**Legumes, Nuts & Beans**
Almonds
Cashews
Chestnut
Edamame
Lentils
Lima beans
Pine nuts
Sword jackbean
Tofu (soft, firm, dried)
Natto
Walnuts

**Dairy**
Edam cheese
Emmental cheese
Gouda cheese
Jarlsberg cheese
Yogurt
Beverages & Soups

Apple cider
Cocoa powder
Coffee
Green tea
Miso
Soy milk

Sweets
Chocolate
Honey
Maple syrup

Further reading:


http://www.ted.com/talks/william_li.html

http://www.eattobeat.org