# DEVELOPMENT OF CANCER CELLS - GENETIC OR BIOCHEMICAL ORIGIN?

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Professor Bruce Ponder of the University of Cambridge led a study that has opened up the field of chromosomal aberrations and screening mutated genes that increase the risk of developing cancer by up to 60 (NST Tuesday, May 29, 2007, p 27)

The success of the research is its ability to scan large stretches of the human genome through a new technique to assess 200,000 blocks of DNA simultaneously instead of one by one. While that research study concentrated on genes associated with breast cancer the same technique can be used in patients with other forms of cancers. The technique speeds up the rate of gene identification, especially mutated genes for a range of cancers and it helps to calculate a woman's predisposition to develop breast cancers over a lifetime.

Certainly, it is an important discovery and all the more important when it is properly understood in terms of preventive medicine. Firstly, there is need to understand what causes genetic mutation and chromosomal aberrations, not just the mechanisms involved but the damage initiated at the molecular and submolecular level. It is clear that while secondary free radicals such as the peroxynitrite radical tend to cause oxidative damage to cell membranes the hydroxyl radical, produced by the reaction between the superoxide and hydrogen peroxide produced during cell metabolism can oxidatively damage the DNA molecule by attacking the hydrogen bonds. Enzymes involved in the replication of genetic material can also be oxidatively damaged by oxidative stress produced by both the peroxynitrite and hydroxyl radicals.

So, the first point to note is that people with genetic mutations have had their genetic material exposed, at some point, to excess free radicals or chemical stressors or drugs that generate free radicals in the body.

ATP is the energy molecule produced through aerobic respiration that yields cellular energy. This process uses oxygen and the ATP molecules are produced by the Krebs cycle that is dependent on antioxidants – it is an antioxidant-driven cycle in the mitochondria. Excess superoxide in the cytoplasm tends to raise the acidity that shuts down the antioxidant enzyme system involved in the Krebs cycle and that can favor the rerouting of the glucose molecule through another pathway that yields alcohol as the energy molecule of the cell. When the Krebs cycle is shut down, ATP is not produced, but the cell needs energy and it resorts to rerouting glucose through another pathway to produce alcohol. The breakdown of alcohol yields energy and when the cell is able to produce alcohol and breaks it down for its energy needs, it effectively is transformed into a cancer cell.

Hence, strictly speaking, it is not the genes or mutated genes that cause cancer. The real cause is biochemical in nature that depends very much on the free radical-antioxidant equilibrium wherein excess free radicals lead to oxidative stress and oxidative damage. Mutated genes and chromosomal aberrations do not by themselves cause the formation of cancer cells but indeed when these are present, the risk of developing cancers increases and quite rightly, there is no direct link but it serves as a clue to predisposition to cancers.

Studying a rare inherited syndrome, researchers at Johns Hopkins have found that cancer cells can reprogram themselves to turn down their own energy-making machinery and use less oxygen, and that these changes might help cancer cells survive and spread. The Hopkins scientists report that the loss of a single gene in kidney cancer cells causes them to stop making mitochondria, the tiny powerhouses of the cell that consume oxygen to generate energy. Instead, the cancer cells use the less efficient process of fermentation that yields alcohol, which generates less energy but does not require oxygen (anaerobic respiration). As a result, the cancer cells must take in large amounts of glucose (Huafeng Zhang et al, University of Chicago;ref, Science Daily, Cancer Cells 'Reprogram' Energy Needs To Grow And Spread, May 8, 2007). In essence, there is a switch in the pathway that yields cellular energy which involves the rerouting of the glucose molecule into the fermentation process to produce alcohol.

There are studies that have documented a relatively high population of free radicals in people with trisomy-21 and other similar aberrations. Also, diabetics whose blood sugar levels are high also have relatively higher populations of free radicals in their body quite similar to obese people as free radical scavenging activity in fatty tissue is much slower that in the watery medium. Hence reducing abdominal girth as a way to reduce visceral fat tends to improve blood chemistry and reduces risk of cancers. Another recent study clearly indicated that diabetics have a high incidence in fertility problems and risk damage to membranes and the DNA in spermatozoa. This observation ties in with the relatively high populations of hydroxyl radicals that can damage DNA molecules in spermatozoa.

At the biochemical level, how is this clue to a predisposition to cancers explained? Well, normal and undamaged genes produce normal biomolecules that are neutral or they may produce antioxidant molecules. Some types of damage to the genetic material may slow down cell division but some types of damage in mutated genes may produce abnormal molecules that act like free radicals and can initiate free radical chain reactions or produce localized damage to cell membranes and aid the accumulation of the superoxide in the cytoplasm by depleting the antioxidant enzymes within the cell or impairing anything that leads to a significant drop in ATP production and the switch in the energy pathway takes place leading to the formation of the cancer cell. We know that cancer cells can produce alkanes and alkynes but the issue of abnormal molecules and abnormal proteins formed in cells under oxidative stress is of special interest in medicine.

The fundamental mechanism that alters how the cell’s energy molecule is produced and whether it is ATP or alcohol depends on oxidative stress on the Krebs cycle. There is no genetic mechanism that directly reprograms cells to turn down their aerobic respiration in

favor of anaerobic respiration. The shut down of the production of ATP molecules can also be on account of depletion of mDNA or oxidative damage to the cytochrome system or the impairment of the metallothionein (MT) protein system or depletion of mitochondria in cells caused by oxidative stress or caused by loss of a gene that stops cells from making mitochondria.

From this perspective, the scanning test devised by the Cambridge research team has wide implications in routine scanning for preventive medicine. Once the predisposition has been identified, a diet that ensures a high intake of natural antioxidants and the elimination of trans-fatty acids and TOFU and long-chain fatty acids, elimination of cigarettes and alcohol and elimination of food with synthetic preservatives and synthetic vitamins will naturally reduce the risk of developing cancers.

Cancer researchers however have long known that cancer cells are distinguished from their 'normal' cousins by an alteration of the cells' energy metabolism. The mitochondria inside the cells become inactive and the cells switch to a secondary mode of energy production that is based on the fermentation of sugars. This metabolic change has recently been confirmed by a study at Johns Hopkins. This point about cellular energy produced aerobically through antioxidant-driven pathways is the key to preventing and treating cancer patients.

Studying a rare inherited syndrome, the researchers at Johns Hopkins found the loss of a single gene in kidney cancer cells causes them to stop making mitochondria, the tiny powerhouses of the cell that consume oxygen to generate energy. Instead, the cancer cells use the less efficient process of fermentation, which generates less energy but does not require oxygen. As a result, the cancer cells must take in large amounts of glucose to get the same amount of energy through the anaerobic process that uses less oxygen and that these changes might help cancer cells survive and spread (see:Huafeng Zhang et al, University of Chicago;ref, Science Daily, Cancer Cells 'Reprogram' Energy Needs To Grow And Spread, May 8, 2007).

It is about how the energy is produced - either from routing glucose through the Krebs cycle to produce ATP or rerouting of the glucose molecule through the anaerobic pathway to produce alcohol as the new energy molecule that cancer cells use.

The rerouting of the glucose molecule may take place when the mitochondria are depleted in cells which mean a dramatic decrease in energy from ATP. The depletion of mitochondria can be initiated by loss of a gene involved in the process of making mitochondria or oxidative damage to such genes by hydroxyl radicals or depletion of mitochondria by oxidative stress on the process for making mitochondria. Also, the rerouting can take place when the acidity of the cytoplasm increases by accumulation of the superoxide (oxygen free radical) that inactivates the enzymes involved in the Krebs cycle and the production of alcohol starts the life of the cell as a cancer cell.

The mitochondrial depletion mechanism explains the tiredness or chronic fatigue as observed in AIDS patients and both these mechanisms explain the development of

cancers in patients who have suffered the symptoms of AIDS for a long period of time which is consistent with expected effects of prolonged oxidative stress. Consequently a cocktail of natural antioxidants that incorporate medium chain fatty acids will have a positive effect especially in the early stages where reversal is much easier to achieve.

The use of turmeric or other spices, singly or in combination, effectively scavenges the superoxide inside the cancer cells and also disrupts the free radical-driven iron sulfide pathway that is so essential to the development of pre-malignant cells (that lose the glutathione in them to the cancer cells) and aids the development of tumors. One way to treat cancer patients is to destroy the iron-sulfide pathway in cancer cells which may be achieved by the use of spices and grapeseed oil.

The research at Johns Hopkins confirms what I have written in these columns about the switch in the energy pathway and the production of another energy molecule that yields energy less efficiently. The mitochondrial origin of disease is also true and it also has to do with ATP production through the cytochrome enzyme system and if the protonation process is disrupted by excess free radicals there is disruption in the production of ATP and also leads to tiredness or chronic fatigue as well. Oxidative damage to the membranes of the mitochondria is also a factor in the mitochondrial origin of cancers and explains why some people with AIDS symptoms develop cancers.

The MT protein system in the mitochondria functions to bind the hydroxyl radical produced inside the mitochondria and transports it out of the cell. Naturally, oxidative stress on the MT protein system that sufficiently impairs it can also be a factor in lowering mitochondrial output and lower ATP production or leads to the inactivation of mitochondria altogether and they disappear which becomes a factor that favors the switch to anaerobic pathway.

Hence, cancer cell development and tumor development occur in consequence to oxidative stress, rerouting of the glucose molecule into an anaerobic biochemical pathway that is toxic and the establishment of toxic pathways that are free radical-induced lead to tumor development and their progression when they become free radical bioreactors. Cancer is certainly a metabolic disorder that involves how cellular energy is produced in cells.

Heinrich Kremer's hypothesis of a photon-mediated cellular energy pathway is interesting but it does not seem to hold at the biochemical level. And it would require more research to ascertain the value of this hypothesis. Perhaps experimental research using photons may shed some light. It must be pointed out that photons play an important and critical role in the biochemistry involved in photosynthesis where photons from sunlight are involved in the electron transfer process through chlorophyll. In humans the hemoglobin is the molecule that is closest to chlorophyll but it does not play a role in the biochemistry in the cytochrome system or in the protonation process in mitochondria or in the electron transfer process.

The most interesting part of Heinrich Kremer's hypothesis is the attention he draws to the the function of the adenine groups of ATP as no biochemical reaction with this adenine ring molecule is shown. There is resonance in the adenine group of the ATP molecule which is a unique rotation system to the adenine group of ATP whose electrons can move freely in the alternating double bonds of the ring molecules. A change in the quantum of energy in this ring can possibly produce a dynamic transfer of electrons and as such it becomes an interesting biomolecule that can scavenge free radicals inside the mitochondria and improve cell function and cell output. A benzene ring on the other hand quite possibly works in just the opposite fashion by robbing electrons from antioxidant molecules.

The ability to transfer electrons through excitation by photons would also mean that it can contribute to the protonation process (ie formation of protons in the cytochrome system). This biochemistry appears to clearly explain why phototherapy works in newborns that have jaundice as it would certainly improve liver function and helps explain the formation of vitamin D in the skin from its precursor, ergosterol, by the action of sunlight. Quite possibly it is an important molecule in the repair of cell membranes. Oxidative damage to cell membranes can lead to the development of cancers or promote the spread of the cancer.

Equally interesting is his observation that “all essential components of mitochondrial cell respiration are light absorbing molecules with characteristic “frequency windows” of absorption maxima from nearly UV spectrum to the longer wave yellow/orange spectral range of visible light up to ca. 600nm. Yet the source of the electromagnetic energy is not sunlight. In fact a low frequency pulsating electromagnetic field is induced by the constant flow of uncoupled, paramagnetic aligned electrons in the respiratory organelles.” This also explains why electromagnetic resonance as used in the cytotron helps to promote regeneration of cartilage and bone tissues in the arthritic knee which achieves better results with the administration of natural free radical scavenging antioxidants such as by administering natural antioxidants through a cocktail of fruit juices and possibly krill omega-3 fatty acids to further support repair of cell membranes. This would mean that the adenine group of the ATP molecule can also accept electrons from some of the other antioxidant enzymes, notably CoQ10. That, in turn should encourage patients undergoing treatment with cytotrons to also consume fresh vegetables together with the fruit juices shortly before starting each treatment. Curcumin, the key antioxidant in turmeric, may have a special affinity for the adenine group of ATP and it is readily able to transfer electrons into it and recharges it and works in this network just as how the other natural antioxidants work in a network fashion by giving electrons to recharge a “spent’ antioxidant. In this manner curcumin boosts the antioxidant role of the adenine group of ATP effectively which promotes the aerobic respiration process. In this regard, curcumin helps to prevent depletion of CoQ10.

This new field of information taken together with the Johns Hopkins research, if it is accepted in medical science, it becomes obvious that further research into natural antioxidants from food or edible substances is desirable to find interventions to boost the

natural antioxidant defense mechanism and in the use of such molecules or in the nano form to induce free radical scavenging activity rapidly that

1. help to terminate free radical chain reactions, and

2. help to suppress or terminate the iron-sulfide pathway, and

3. help to rapidly repair cell membranes including repairing of the cell wall to reduce and eliminate the positive charge on the cell wall, and

4. help to rapidly reduce the acidity levels in the cytoplasm to reactivate the Krebs cycle and production of ATP aerobically by scavenging the superoxide in the cytoplasm or prevent lactate build-up, preferably by the use of natural antioxidants, and

5. help to reestablish the healthy antioxidant-driven pathways, or otherwise

6. selectively kills cancer cells and do not harm but instead promote the healthy biochemical pathways in normal and healthy cells.

When looking at the production of abnormal proteins in cells that can lead to disease states, one starts by looking at the genetic material as a system of information that also codes for inheritance. A dolphin breeds dolphins. A bear breeds cubs that will grow and develop into bears. Acorns from an oak tree, when planted, will produce oak trees. A hibiscus cutting will grow into a whole plant that is also a hibiscus. Creatures and plants remain true to type, faithfully passing on their characteristics from generation to generation. In humans, one chromosome of each pair is inherited from the mother, and the other comes from the father. This is why children resemble their parents, both physically and in their tendency to develop certain diseases. It must be remembered that it is tendency. The mechanism of inheritance is carried faithfully through the genes unless the genes mutate or suffer damage which we call genetic aberration or chromosomal aberrations when whole chromosomes are involved and there are other newly discovered mechanisms involved that can lead to the development of disease conditions.

We know that the hundreds to thousands of genes are arrayed on the chromosomes. Genes are segments of DNA that code information for cells to read and do a specific task, usually to make a particular protein. Each protein has a specific job or function in the body; for example, some proteins help muscle cells contract. Each human cell has about 30,000 genes; each one makes a protein with a unique function.

Genes store information that is arrayed in sequences and encodes information for the synthesis of molecules including proteins. Genes encoding proteins may be composed of two or more identical polypeptide chains. A haploid mutant could produce an abnormal polypeptide that assembles into an inactive homomultimeric protein. On the other hand, if two different abnormal polypeptide chains are produced in a heteroallelic diploid strain, the abnormal peptides could assemble in certain combination to produce a catalytically active multimeric protein. In such cases, the abnormal polypeptide chains in some way

mutually compensates for each other's defect (Broach, J. R., Jones, E. W. and Pringle, J. R. (Eds.): The Molecular and Cellular Biology of the Yeast Saccharomyces, Vol. 1. Genome Dynamics, Protein Synthesis and Energetics. Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1991; Brown, A. J. P., and M. F. Tuite (Eds). Yeast Gene Analysis. Methods in Microbiology, Vol. 26, Acad. Press, NY, 1998: DeRisi, J. L., V. R. Iyer and P. O. Brown. Exploring the metabolic and genetic control of gene expression on a genomic scale, Science 278, 680-686, 1997).

While most recessive missense mutations produce an overall misfolding of proteins, dominant-negative mutations retain at least portions of the structure, thus revealing specific critical regions. Dominant-negative mutations can also act in heterozygous diploid strains with one copy of each allele. Such mutant proteins generally have a higher than normal affinity for a cellular component, and displace the wild-type protein. For example, numerous nonfunctional CYC7 mutations were at least partially dominant because the altered forms of cytochrome c were arrested at one of the steps in mitochondrial import or heme attachment, and prevented entry of the normal form (Guthrie, C. and Fink, G. R. (Eds.): Methods in Enzymology, Vol. 194, Guide to Yeast Genetics and Molecular Biology. Acad. Press, NY,1991). So apart from abnormal proteins, mutations in genes can also result in altered enzymes.

Researchers have also figured out how short stretches of DNA that do not normally code for proteins worm their way into genes. This can result in the production of abnormal proteins and lead to genetic diseases, such as Alport Syndrome, a rare kidney disease. But the sequences, sometimes called “junk DNA,” have also allowed humans and other species to create new proteins in a process that has dramatically influenced evolution. Gil Ast and his colleagues at Tel Aviv University in Israel have figured out how the sequences, known as Alu elements, are incorporated into genes to create novel proteins. More than 300,000 sequences are poised for insertion into genes — all that’s needed is a single mutation (ref:Nancy T, Genome News Network, “Junk DNA” Creates Novel Proteins, May 30, 2003). Mutations are changes in the arrangement of the bases that make up a gene. Even a change in just one base in the thousands of bases that make up a gene can have a profound effect.

Mutations occur in our cells off and on. Usually, the genes that "proofread" can recognize and repair the abnormality. If it can’t be repaired, the cell will actually begin a process called apoptosis that leads to its death. That is safety mechanism. More mutations tend to occur under conditions of oxidative stress.

Alu elements are short sequences of DNA that are peppered throughout the genome. They comprise approximately ten percent of the entire genome—ten times more than all the genes put together. Until recently, their function had remained a mystery. One of the biggest surprises to come from the sequencing of the human genome was that we have about 30,000 genes but produce approximately 90,000 proteins. And 99 percent of our DNA codes for no protein at all.

The new research provides a clue as to why we have so much “junk DNA.” It also suggests an explanation of how so few genes can produce so many proteins. Through a process called alternative splicing, humans create multiple versions of a gene and, consequently, multiple proteins. It’s a way of constructing a new protein, while keeping a backup copy of the original version (ref:Nancy T, Genome News Network, “Junk DNA” Creates Novel Proteins, May 30, 2003). When the body creates multiple versions of a gene under the conditions of oxidative stress, particularly in the presence of excess hydroxyl radicals which can damage hydrogen bonds in genetic molecules, the encoding sequence is tampered and it may encode for abnormal proteins.

In the past few years researchers have unearthed a series of genetic abnormalities that contribute to epilepsy. The discoveries are increasing the understanding of the disorder and highlight new, specific ways to prevent seizures. Inherited from our parents, genes guide the production of proteins, which direct the development and function of our brain. Researchers have long suspected that epilepsy sometimes has a genetic component because the disorder can run in families. Recently studies in humans and animals have helped confirm these beliefs. Scientists have identified more than two dozen genes that contribute to epilepsy (ref:Brain Briefings, Society Of Neuroscience, Sept 2004).

One gene termed doublecortin normally produces a signaling protein that helps brain cells find their proper locations during development. An abnormality in this gene hinders the protein production and causes the cells to stop short of their final destinations. This creates the formation of an extra brain layer, very abnormal brain cell messaging, and seizures (ref:Brain Briefings, Society Of Neuroscience, Sept 2004). So, abnormalities in a person's genes, which guide the production of proteins, can play a critical role in the development of the disorder epilepsy (Poolos NP, et al, Neurology, 2002; 58:1559-1562).

There are other disorders that arise from the production of abnormal proteins in the body. Ehlers-Danlos syndromes is a group of disorders which share common features including easy bruising, joint hypermobility (loose joints), skin that stretches easily (skin hyperelasticity or laxity), and weakness of tissues.

The Ehlers-Danlos syndromes are inherited in the genes that are passed from parents to offspring. They are categorized according to the form of genetic transmission into different types with many features differing between patients in any given type.

The fragile skin and loose joints is often a result of abnormal genes that produce abnormal proteins that form an inherited frailty of collagen (the normal protein "glue" of our tissues). In 2001, researchers discovered a new form of Ehlers-Danlos syndrome that is caused by an inherited abnormality in a protein other than collagen that also normally plays a role in binding together the cells of our tissues (including the skin, tendons, muscle, and blood vessels). Abnormalities in this protein, called tenascin, also lead to a form of Ehlers-Danlos syndrome (William C. Shiel Jr., MD, FACP, FACR, Ehlers-Danlos Syndrome, MedicineNet, June 12, 2007). Another good example of a disease condition produced by abnormal proteins is cirrhosis of liver which can be produced by

chronic and prolonged oxidative stress in the liver by cigarettes and alcohol and drugs as well.

Cells switch on and off their genes selectively – activating or "turning on" the genes that provide the required information and may shut it down when their function is not required. This process allows for the different kinds of cells needed to make up different organs like the brain and the liver. And some genes are activated all the time to continuously produce proteins needed for basic cell functions.

Certain proteins help one cell divide into two, while others prevent the cell from dividing too often. We know that mutations can alter the information that is encoded for making proteins in cells and such alterations can result in abnormal proteins. A mutated gene may encode for an abnormal protein, which no longer functions properly. This may not have any effect at all, or it may lead to a disease. If the mutation occurs in a gene that helps control how often a cell divides or one that checks for errors in cell division, it may contribute to a person developing cancer (American Cancer Society, Oncogenes and Tumor Suppressor Genes, 2007: Pierotti NA, Schichman et al, Oncogenes. In: Bast RC, Kufe DW, Pollock RE, Weischselbaum RR, Holland JF, Frei E, eds. Cancer Medicine. Hamilton, Ontario: BC Decker Inc; 2000: 56-66: Park and Vogelstein, Tumor-suppressor genes In: Kufe et al, eds. Cancer Medicine. 6th Ed. Lewiston NY: BC Decker; 2003: 87-106: Ringer and Schniper, Principles of Cancer Biology. In: Lenhard RE, Osteen RT, Gansler T, eds. Clinical Oncology. Atlanta, GA: American Cancer Society; 2001: 25-30).

Some women with breast cancer have an abnormal protein like the HER2/neu protein that promotes excessive growth of cancer cells.

One approach to bring about remission in cancer patients is in the discovery and use of drugs that suppress or interfere with these abnormal proteins, especially the proteins that promote uncontrolled cell division. A drug recently approved by the FDA, called Gleevec (STI571), interferes with the action of the abnormal bcr-abl protein in chronic myelogenous leukemia cells. This drug has led to remission of the leukemia in almost all patients treated in the early stages of their disease. Similarly another drug was found to be useful in treating women whose breast cancer cells that have abnormal proteins. So, testing for abnormal proteins is a good diagnostic test but after the remission it is essential for the patient to consider a high intake of antioxidants through a diet that ensures a broad range of natural antioxidants. There is scope, in certain cases for integrative medicine that must be supported by regular testing for abnormal proteins. Integrative medicine in such cases would devise a modulation wherein a few days of suppression of abnormal proteins is immediately followed by high antioxidant therapies that can promote normal and healthy pathways that yield normal proteins.

The safer approach in antioxidant therapies may lie in firstly to scavenge free radicals rapidly and supported by high antioxidant blood levels to preserve or promote antioxidant-driven pathways that yield normal proteins and to always maintain an excess antioxidant equlibria in the blood that ensures effective free radical scavenging activity to prevent oxidative damage to the genetic molecules. That sums up the preventive measure

to maintaining good health which corroborated by the many epidemiological studies that show that populations with high antioxidant intake have lower risk to cancers or diabetes or cardiovascular disease. A diet rich in antioxidants and some amount of medium chain fatty acids will probably become the preferred diet to lower risks to disease states in the years ahead.

In conclusion, it can be said that health is promoted by always having an excess of antioxidants, in excess of the amounts required to scavenge the superoxide and hydrogen peroxide formed in cells during their normal metabolism so that secondary free radicals, such as the peroxynitrite and hydroxyl radicals are not formed so that there is no oxidative damage to cell membranes, molecules in the body and no such damage to the genetic molecules and no impairment of the MT protein system while antioxidant therapies aim to repair the oxidative damage to membranes, molecules and the MT protein system in order to restore optimal cellular function and restore the production of normal molecules and normal proteins and promote aerobic respiration to yield sufficient amounts of ATP molecules and enhance the production of repair proteins. That approach is entirely in line with modern science in the field of biochemistry and cellular biology. It can form the central concept in modern health science.

In 1979, Robin Willson and colleagues at Brunel University (working with CRC support) showed using pulse radiolysis that after vitamin E (vit-E(OH)) has repaired oxidative damage by donating its hydrogen atom, it can itself be restored to carry out more radical repair reactions by reaction with vitamin C (ascorbate, $AH^-$ ) (see: Review Article: Free Radicals: nature's way of saying NO or Molecular murder, !993, Gray Lab Annual Rep; Gray Lab Cancer Research Trust). Hence, antioxidants must be used in combinations and formulated as such so that they work in the same manner as the antioxidant network system in the body.

In Fenton Medicine, the aim is to achieve this repair more rapidly through rapid free radical scavenging activity and the sprays may be formulated to also contain curcumin extracts in the nano form from leaves or roots of the plant. In ayurveda and village medicine in India, curcumin is also used in wound healing. Now we know why.

The concept of health and healing at the molecular and submolecular levels has changed in modern medicine. Health benefits have given way to pharmaceutical benefits. Driven by the need to register patents as a way to protect their business, pharmaceutical companies have gone strongly into drugs and synthetics but keep a keen interest on phytochemicals and how natural antioxidants may be used in the therapeutic applications provided they can fit their products into laws that might protect their business interest.

Watchful health and medical authorities continue to link the prestige of medicine with pharmaceutical benefits and some may continue to hold the view that modern medicine must not abandon the notion of only administering pharmaceutically prescribed drugs to achieve pharmaceutical benefits in patients. Drugs can be toxic as they can generate a large number of free radicals and promote the formation of secondary radicals in the body and their long term use can promote the development of disease conditions. The drug,

tamoxifen, was widely used since 1970 to fight breast cancer because it was shown to bind onto the estrogen receptor in cancer cells and thus thought to impede tumor growth and results showed it was very efficient in treatment of most breast cancer patients. However, its capacity to generate free radicals in the body can also lead to negative effects which may be due to oxidative damage to such receptors in normal cells or it can generate sufficient amounts of hydroxyl radicals to cause oxidative damage and perhaps alter the genes involved in cell division or the drug could be generating superoxides by reacting with the glutathione disulphide radical-anion, keeping in mind that tumor cells are rich in glutathione.

In thiol biochemistry, Gerald Adams and his colleagues (whilst working in the Gray Laboratory in 1967) is noted for their observation in a reaction which produces the glutathione disulphide radical-anion by pulse radiolysis of reaction of GS· with glutathione itself, The latter reacts extremely rapidly with oxygen and produces superoxide radicals (Review Article: Free Radicals: nature's way of saying NO or Molecular murder, !993, Gray Lab Annual Rep; Gray Lab Cancer Research Trust) and may explain how the iron-sulfide pathway is maintained as a free radical-induced pathway and why cancer cells draw glutathione into themselves from normal cells surrounding them and helps promote the growth of the tumor.

Hence, even the administration of bioreductive drugs which are used on the basis for the selective toxicity towards hypoxic cells where its action is ascribed to activation of the drug to a free-radical intermediate reactive towards oxygen can work to kill the cancer cell or promote tumor growth. Such drugs are only effectively reduced to a toxic product at low oxygen concentrations, viz, in cancer cells which are hypoxic cells and on the face of it appear to be targeting cancer cells but in reality their superoxide generating capacity supports the iron-sulfide reactions in cancer cells and help maintain the acidity of the cytoplasm that inactivates the enzymes involved in aerobic respiration. And that action promotes cancer cell formation and promotes tumor growth if it cannot kill the cancer cell. It points to the answer why there is no such thing as chemo-cure but remission and relapse in many of the cancer patients.

According to new research at the Malmo University Hospital, UMAS, in southern Sweden, the drug can have the opposite effect on certain types of tumors and in some cases it can actually stimulate tumor growth and increase the likelihood of relapse (Malay Mail, 2/9/2005, AFP: cancer research, 2005). In attempting to harness the pharmaceutical benefits of drugs, modern science also requires that their effects at the molecular and cellular be also studied to determine their health hazards. It is just part of scientific temper that encourages evidence based medicine.



This article forms a chapter in a forthcoming book titled FENTON MEDICINE.