Alternative and Integrative Oncology

The Reference Guide to Evidence Based Cancer Therapies

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FOREWORD

Alternative and Integrative Oncology is a long-awaited reference guide to evidence based alternative and integrative cancer therapies. The author, Dr. Greg Fredericks draws on 5 years of investigation and over 30 years practice experience to produce this evidence-based compendium of over 300 topics and treatments from around the world.

It is designed for naturopathic oncologists, practitioners of naturopathic medicine and cancer researchers but is also a useful tool for anyone who is interested in pursuing alternative cancer treatments or for augmenting orthodox treatments.

The book provides a special dimension, not often encountered, in the form of very interesting, illustrated, historical research that recognises the contributions and thinking of some of the greatest names in medicine.

An important feature of the text is the enormous amount of very practical, useful information in an alphabetically-arranged list of treatments and interventions to assist practitioners and cancer sufferers. It provides an efficient, quick reference guide to an impressive range of cancer therapies with an emphasis on evidence-based validation drawn from human and animal studies and case reports. Also provided is a table of botanical cytotoxic isolates as well as anticancer synergistic plant metabolites. However, it also draws on useful testimonials, anecdotal evidence and folklore reports – all seen in present-day scientific context. This is enhanced by a table at the back of the book that outlines complementary homoeopathic medicines including those with peer review validation.

The book commences with an introduction to the important new field of naturopathic oncology and an overview of very important fundamental concepts about the origin of cancer; cancer myths that influence clinical decision-making and should therefore be reconsidered; the cancer personality and the mind-body connection – particularly the link between stress and compromised immunity. The presence of the nagalase enzyme in many forms of cancer is considered; and a range of recent discoveries at prestigious research centres are reviewed. Activation of apoptosis pathways to lead to cancer cell death is explored in detail and excellent coloured plates illustrate important concepts. This is enhanced by a table at the back of the book that consists only of human cancer cell types and pro-apoptotic agents.

A practical overview of carcinogenic food and environmental sources of cancer provides helpful information for practitioners to pass on to patients and to stimulate further investigation into the prevention and mitigation of cancer through nutritional and environmental medicine.

The author's painstaking research and observations have resulted in his magnum opus which is a blend of evidence-based integrative medicine, a review of historical scientific medicine and naturopathic principles presented without any influence from special-interest groups and without any corporate remuneration. The book meets the author's humanistic objectives to save lives and improve the quality of life and increase the scope of available treatments for cancer sufferers; and does this through an evidence-based, scientific approach. Dr. Fredericks is to be congratulated on achieving such a detailed, evidence-based and clinically user-friendly work in a field of medical practice that impacts greatly on the lives of millions.

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PREFACE

It is difficult to conceptualize that a healthy person produces on average, 100,000 cancer cells every day.

A normal functioning immune system works to eliminates potential hazards as part of its daily routine. Factors such as stress, diet, environment and lifestyle choices play a role in how well the immune system is able to eliminate abnormal cells.

People living in modern developed countries are exposed to enormous immunosuppressive conditions as never before. In Australia in the 1990's statistics for cancer incidence were reported to be 1 in 18. Today reports say 1 in 3 and similar statistics are held in other developed countries. It makes one wonder what the statistics will be in the next decade.

There are apparently over 200 different types of cancer with new discoveries happening continually. The term "alternative" however has evolved into 'Integrative Medicine' where doctors are now embracing many of the treatments that are found in traditional and folklore medicine. This has been partly due to the principles of supply and demand. More people simply demand natural treatments today.

The old debate as to whether cancer is a localized disease or a systemic disease seems to have now shifted to a more systemic model in recent years. However mainstream medicine still removes cancer from bodies like removing mould from cheese. There is new understanding about cancer emerging, for instance prostate cancer once thought to be a cancer you die from is now thought to be a cancer you die with, in most cases. This is only one example of where a rethink of strategies has affected protocols in use today.

The intention of this book is a simple one. To help save lives, improve quality of life and expand the scope of treatments currently being offered through an evidence based approach. One of the learning curves from researching the material presented here is that many therapies can be used on their own but also have significant synergistic effects with conventional therapies. Not only can some natural compounds reduce side effects but can increase efficacy in chemo-resistant tumors. In this case western orthodox medicine has some catching up to do to attain the levels of natural augmented treatments in China and Germany. Nevertheless America, Canada and Australia are continuously developing new high-tech innovations and adopting integrative approaches in oncology.

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INTRODUCTION

Dear Reader,

The following is a compendium of natural and integrative oncological treatments. Some may be helpful and effective for certain individuals while others may be totally ineffective. This book does not rate or recommend any particular treatment for any specific type of cancer. The purpose of this book is to briefly describe various treatments and the research that accompanies them. It in no way infers that any treatment protocol is superior to another however the level of research may be worth considering. There are many paradigms of thought used in the various alternative treatments. Some are based in quantifiable biological science while others are based in folklore and/or anecdotal evidence. In some cases the folklore medicines of the past have become the cytotoxic pharmaceutical drugs of the future.

Some treatments listed here are if one already has cancer while others are of a preventative or adjuvant quality. Some treatments can be used to enhance conventional treatments while others cannot. If you have cancer or wish to help someone who has, it is recommended that you see a health professional who is a member of a recognized government approved association. This will ensure that all credentials have been thoroughly scrutinized. The author recommends that to be successful in treating cancer one must investigate what is promoting or creating it.

The reason why people are interested in alternative cancer treatments is largely due to the few options and harsh side effects that orthodox medicine offers. The hope is that orthodox medicine can implement protocols using some of the chemosensitizing herbal constituents presented in this book to improve outcomes with fewer side effects. This will enable an integrative approach using lower doses of chemotherapeutic drugs and enhance quality of life for oncology patients.

The claims made by the information provided is not from the author, but those who have developed and tested the treatments. The author has only provided a summary of information to the reader and it is inevitably up to the reader to decide if they wish to take it further. The tables in the back of this book will provide a quick reference whereby one can check what herb or isolate is cytotoxic to an individual cancer cell type. This information is an invaluable evergrowing resource for professional oncologists, doctors, naturopaths, patients and cancer researchers.

The cancer diet is always a concern for patients; there are many twists and turns to consider. These are discussed as well as theoretical concepts, potential pitfalls and interactions. There is also an eclectic mix of notable people who have influenced the course of cancer history. The information in this book is compiled from an objective evidence-based approach without influence from special interest groups.

NATUROPATHIC ONCOLOGY

When I started writing this book there was no intention for it to become as extensive as it is today. It started after visiting a friend in Canada in 2012 whose wife was dying of a brain tumor. I started writing down as many natural protocols as I knew at the time to assist the patient and mentioned that cordless/mobile phones might be a factor. Mostly working from a mitochondrial pathway that is still prevalent today, I listed a number of supplements that would give an integrative support to the patient's orthodox treatment. I've done this before for patients but this time I decided to keep the list of protocols and add other ubiquitous remedies for other types of cancers. From this list of 60 supplements and protocols with a brief explanation of each, the book eventually grew to where it is today. As there are new isolates and plant alkaloids being discovered every day throughout the world it soon became apparent that this would be a never ending task. Researchers for pharmaceutical companies are constantly testing the seed, roots, leaf or bark of a plant looking for the constituent that has the most significant apoptotic/cytotoxic effect against specific cancer cells.

I decided I would attempt to compile as many protocols, herbs, isolates etc. for my own personal reference, with no intention to dispense this information to anyone else. However, my interest changed when I heard about "Naturopathic Oncology" in America. This new field of naturopathy has stimulated my interest and I was surprised to find that approximately 80% of naturopaths in Australia choose not to get involved with oncology patients. Cancer seminars for naturopaths have been available since the 1990's but the term "Naturopathic Oncologist" is only a recent term existing since 2006 in America.

These Naturopathic Oncologists are naturopathic physicians from the American Naturopathic Physicians Association that have passed an additional board certification and training and have the initials FABNO (Fellow of the American Board of Naturopathic Oncology) after their ND. One such ambassador and teacher of this new area of Integrative Oncology is Dr. Lise Alschuler ND. FABNO. Dr. Alschuler has appeared at many naturopathic congresses and seminars around the world including Australia.

Dr. Alschuler has presented the current integrative protocols and dietary support for cancer patients with careful consideration to an integrative approach with orthodox oncology. Emphasis on avoiding refined denatured foods, use of ketogenic diets and supportive "orthodox approved" supplementation to increase efficacy of conventional treatments are at the core of current naturopathic oncology. Dr Alschuler has first hand experience of integrative approaches and is an inspiration to others in this field. This book has been inspired by her work and will hopefully help to expand the scope of integrative treatments in the future.

Another international practitioner/lecturer relevant to this field is Daniel Weber PhD, MSc, DSc who has released a ground breaking work called "Botanical Oncology". This Australian Traditional Chinese Medicine professor has contributed a detailed structured guide on plant isolates used in oriental and western approaches in cancer care. He has lectured on modern botanical and functional medicine and has helped to broaden the base of naturopathic oncology throughout the world.

Today naturopathic oncology is still in its infancy especially in western medicine. This is evident by the narrow scope of acceptable adjuvant therapies currently approved for use. Compared to oncology in China, western oncology is only offering a cautious handful of integrative therapies. One can also observe the different approaches in the USSR and Germany and understand why a certain percentage of oncology patients seek help abroad.

In recent years there has been resurgence in German physiologist Otto Warburg's hypothesis on the energy metabolism of cancer cells being different from normal cells. Normal cells make energy by breaking down the 6-carbon glucose to two 3-carbon pyruvate molecules through cytoplasmic glycolysis that does not require oxygen; this in turn creates oxidative reactions in the mitochondria where oxygen is needed.

Cancer cells, however, depend on glycolysis to obtain energy with or without oxygen. It has since been proven that some cancer cells appear to have working mitochondria even though Warburg's hypothesis is mainly a mitochondrial dysfunctional cause of cancer. This is after decades of domination of cancer believed to be a genetic (oncogene) dysfunction. Warburg's postulations have been recently supported by positron emission tomography (PET) imaging findings that cancer tumors have increased glucose uptake. The geneticists believe it is an effect of cancer rather than the cause. In any case, the end product of glycolysis; lactate and acidic compounds contributes to the further breakdown of the extracellular matrix facilitating cellular invasive metastatic processes. Many theories and paradigms have been developed concerning the origin of cancer. The most recent theory of the origin of cancer is that cancer has a viral origin, which is a rediscovery of the work by Royal Raymond Rife in the 1920's. Many researchers now believe viruses cause gene mutations that result in cellular abnormalities. This does not detract from the metabolic genetic phenotype facilitating carcinogenesis.

APOPTOSIS CANCER SIGNALLING PATHWAYS

The process of apoptosis, or programmed cell death is fundamental during normal development and homeostasis, while aberrant apoptosis has been implicated in a number of human diseases including cancer.

Activation of apoptosis pathways is the key mechanism by which cytotoxic agents kill tumor cells. Defects in apoptosis signalling are what contribute to resistance of tumors. Molecular insights into regulation of apoptosis and defects in apoptosis signalling in tumor cells have provided new approaches to deal with resistance of tumor cells for future therapeutic strategies. Some novel approaches using pro-apoptotic plant isolates on their own and in integrative regimens will be discussed in individual remedies throughout this book. The following is a brief overview of the complex subject of apoptotic signalling pathways. A short list of potential methods of anti-apoptotic therapy includes stimulation of the IAP (inhibitors of apoptosis proteins) family of proteins, caspase inhibition, PARP (poly [ADP-ribose] polymerase) inhibition, stimulation of the PKB/Akt (protein kinase B) pathway, and inhibition of Bcl-2 proteins. These will be elucidated in the following discussion.

Activation of the mitochondrial (intrinsic) pathway of apoptosis in addition to signalling through the death receptor (extrinsic) pathways, are what contributes to sensitivity of tumor cells towards a successful cytotoxic treatment. Both pathways converge finally at the level of activation of caspases, the effector molecules in most forms of cell death. The extrinsic pathway of apoptosis signalling is initiated when death receptors at the cell surface encounter specific cognate “death ligands,” inducing a conformational change that is transmitted through the cell membrane. These receptors can activate caspases within seconds of ligand binding and lead to apoptotic cell death in a matter of hours. Three major specific cell death receptor/ ligand pairs have been described, all members of the Tumor Necrosis Factor Receptor Superfamily (TNFRSF): (1) Fas and Fas ligand (FasL) (Fas is also called Apo-1, CD95 or TNFRSF6 ; FasL is also called CD178,CD95L or TNFSF6 (2) “death receptors” (DR4 and DR5) and TNF-related apoptosis inducing ligand (TRAIL, also called Apo2L or TNFSF10and (3) TNFα and the TNF receptor (TNF-R1)(Xu et al. 2007).

The intrinsic pathway of apoptosis signalling is under the control of the Bcl-2 (B-cell lymphoma 2) family of genes and its proteins. It is initiated by intrinsic signals transmitted via intracellular molecular components that also ultimately lead to caspase activation. Our knowledge on how this signal is transmitted is still rudimentary, but we do know that the outer membrane of mitochondria gets directly perforated as a result (Dash et al. 2008).

In addition to classical apoptosis, non apoptotic modes of cell death have recently been identified. Mechanisms to overcome apoptosis resistance include direct targeting of antiapoptotic molecules expressed in tumors as well as re-sensitization of previously resistant tumor cells by re-expression of caspases and counteracting apoptosis inhibitory molecules such as Bcl-2 and molecules of the IAP family of endogenous caspase inhibitors.

Within the IAP family of endogenous caspase inhibitors important for apoptotic processes is a protein called survivin. Investigators interested in mechanisms of apoptosis have found survivin an evolving challenge. Survivin is a member of the inhibitor of apoptosis (IAP) gene family that has attracted attention from several viewpoints of basic and translational research. While survivin inhibits apoptosis in vitro and in vivo, this pathway may be more selective as compared to cytoprotection mediated by other IAPs. Researchers in cancer biology have converged on survivin as a pivotal cancer gene, not simply for its significant expression in tumors but also for the potential use of this pathway in cancer diagnosis and therapy. Survivin is a cell cycle-regulated expression of mitosis and is associated with the mitotic apparatus. It has been of interest to cell biologists studying faithful segregation of sister chromatids and timely separation of daughter cells. Current evidence and emerging concepts on the multifaceted functions of survivin in cell death and cell division has been significant to how this pathway is being pursued for novel cancer therapeutic strategies.

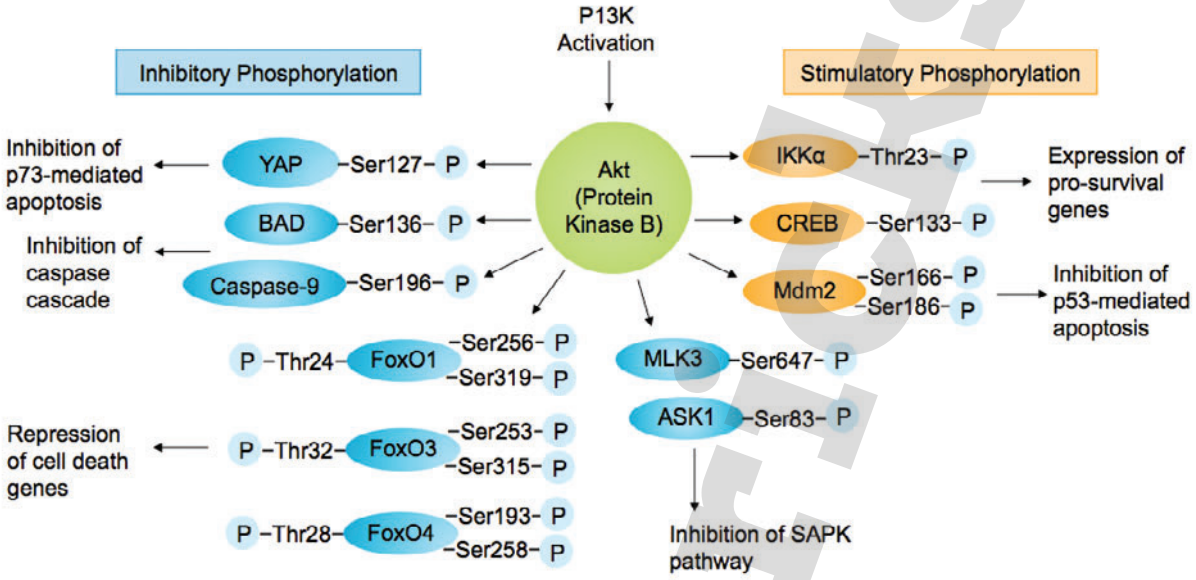
In the subject of apoptosis the p53 must be considered. The p53 pathway has been shown to mediate cellular stress responses and can initiate DNA repair, cell-cycle arrest, senescence and apoptosis. These responses have been implicated in an individual’s ability to suppress tumor formation and to respond to many types of cancer therapy. In particular p53 itself and its negative regulator MDM2- in cancer cells has proven useful in the development of targeted therapies.

The p21 is a p53 transcription target implicated in both major functions of the tumor suppressor-cell cycle arrest and apoptosis. p21 is a potent inhibitor of the key cyclin-dependent kinases (CDK1–4), and has been thought to be the main mediator of p53-dependent G1 and G2 arrest. However, an increasing body of information suggests that in addition to its cell-cycle inhibitory activity, p21 can affect p53-dependent apoptosis.

Regulation of apoptotic mitochondrial events occurs through members of the Bcl-2 family of proteins. The tumor suppressor protein p53 has a critical role in regulation of the Bcl-2 family of proteins. The Bcl-2 family of proteins governs mitochondrial membrane permeability and can be either pro-apoptotic or anti-apoptotic. Twenty-five genes have been identified in the Bcl-2 family. Some of the anti-apoptotic proteins include Bcl-2, Bcl-x, Bcl-XL, Bcl-XS, Bcl-w, BAG, and some of the pro-apoptotic proteins include Bcl-10, BAX, Bak, Bid, BAD, BiM, Bik, and Blk. These proteins can determine if the cell commits to apoptosis or aborts the process.

The dynamic duo of Puma and Noxa are two members of the Bcl-2 family that are also involved in pro-apoptosis. Puma plays an important role in p53-mediated apoptosis. An overexpression of Puma can increase BAX expression, BAX conformational change, translocation to the mitochondria, cytochrome C release and reduction in the mitochondrial membrane potential. Noxa is also a candidate mediator of p53 induced apoptosis. Studies show that this protein can localize to the mitochondria and interact with anti-apoptotic Bcl-2 family members, resulting in the activation of caspase-9. Puma and Noxa that are induced by p53 to mediate apoptosis are thought to be activated by geno-toxic damage or oncogene activation.

It is thought that the main mechanism of action of the Bcl-2 family of proteins is the regulation of cytochrome C release from the mitochondria via alteration of mitochondrial membrane permeability. Interestingly cytochrome C released from the mitochondria is what triggers caspase activation and appears to be largely mediated by direct or indirect ROS action. Reactive oxygen species (ROS) and mitochondria play an important role in apoptosis induction under both physiologic and pathologic conditions. This pathway has been identified as being significant in certain types of cancer such as pancreatic. On the other hand, ROS can also have anti-apoptotic effects in certain circumstances.



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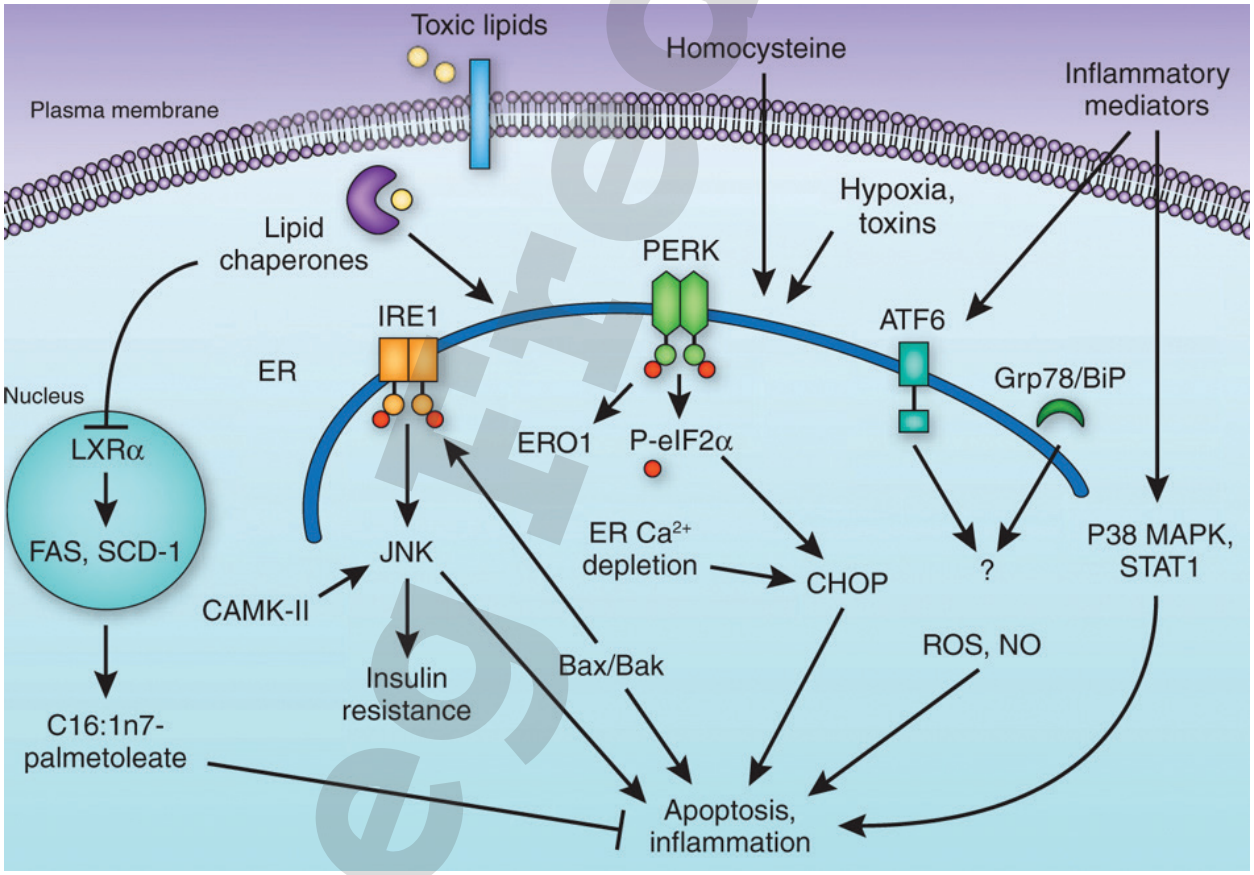

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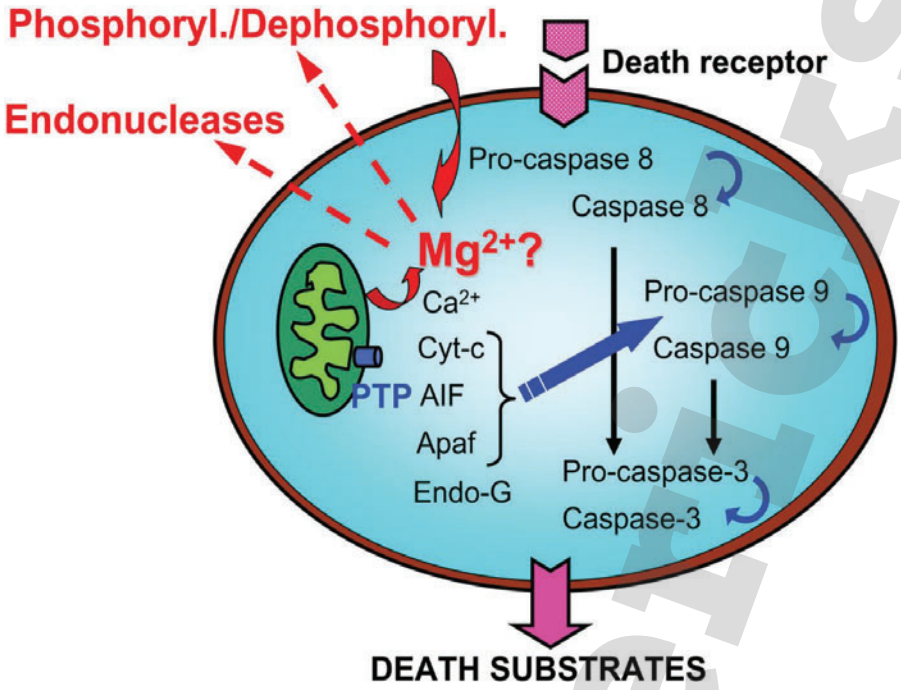

Death Substrates/Pathways of apoptosis and the possible involvement of Mg

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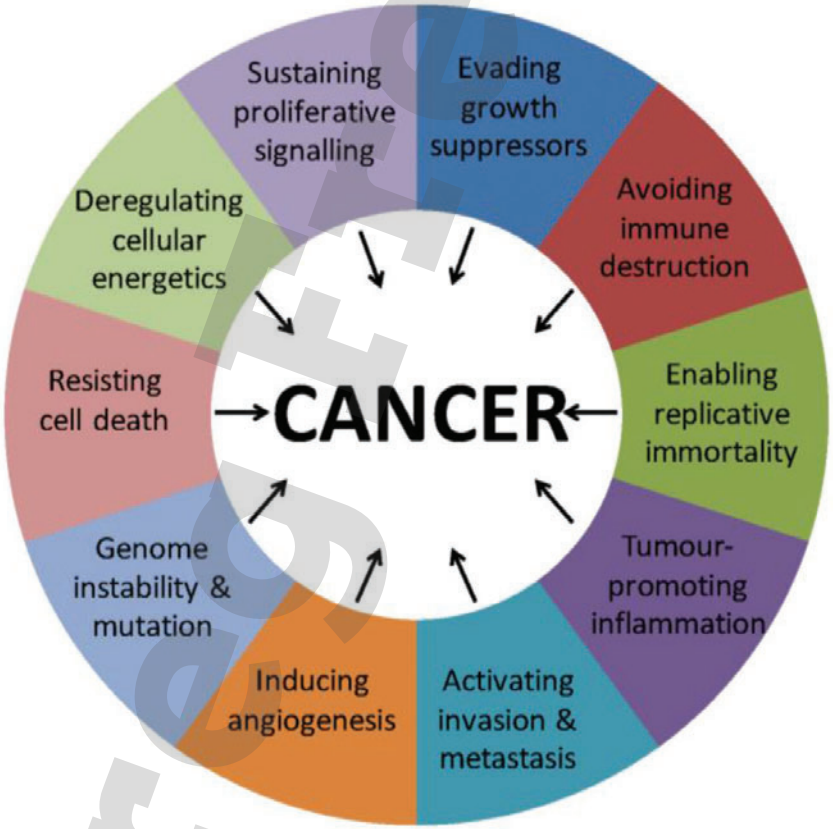
Article: Cell (patho) physiology of magnesium
Publication: Clinical Science Jan 01, 2008, 114(1)27-35; DOI: 10.1042/CS20070129



Hallmarks of Cancer

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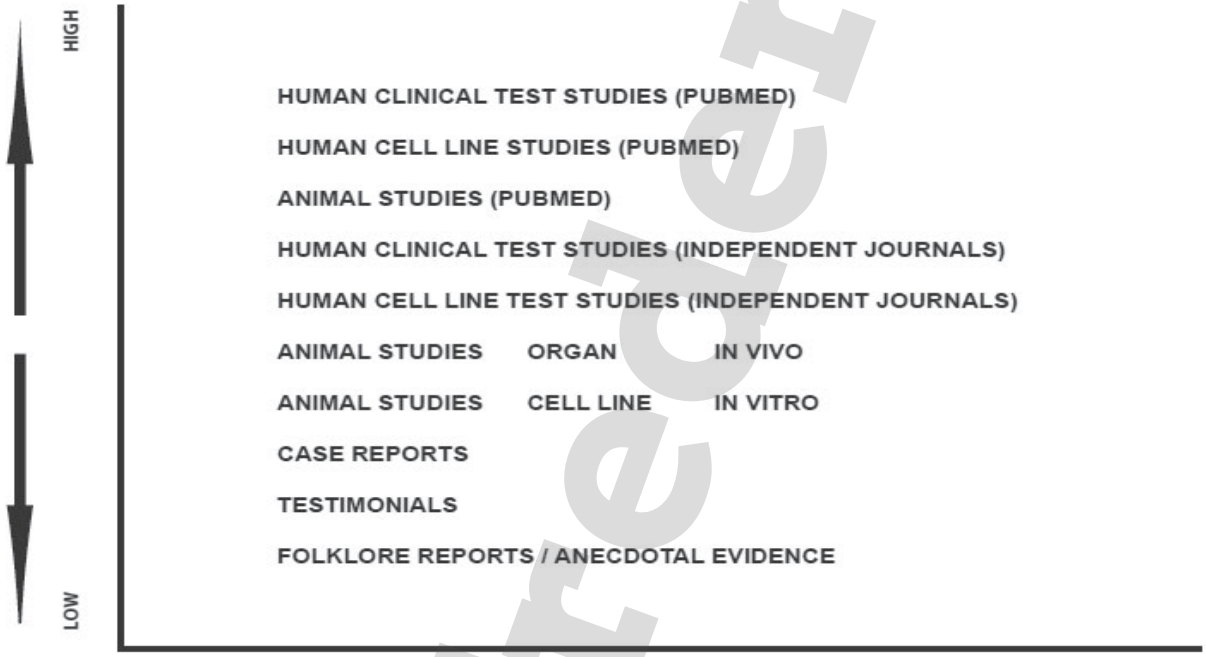
Publication: MDPI Journals -Cancers 2016, 8(3), 35; DOI:10.3390/cancers8030035.

PREAMBLE TO THE TREATMENTS

The following information is a compilation of alternative and integrative treatments and therapies that have been used by people worldwide. Some are based in quantifiable medical science while others are of a more dubious nature. The criteria for what is considered proper scientific validation can be traced back and credited to the Rockefeller family in the early twentieth century. Their influence in medical school curriculum, research, medical and pharmaceutical protocols are still in place today.

A graph has been provided to help those researchers who want to check the reference material for orthodox scientific validation. A few subjects presented in this book may not measure up to an evidence based criteria. PubMed studies are considered admissible in a court of Law.

EVIDENCE DETERMINATION



THE TREATMENTS

The reader must assume responsibility if they decide to use any of the treatments listed. It is recommended to seek the advice of a professional and to do further research in any subject presented here.

AARSOTA BIOLOGICAL VACCINE

AARSOTA is known as autologous Antigen Receptor Specific Oncogenic Target Acquisition. AARSOTA is a cancer vaccine developed from proteins that are produced by cancer cells that are extracted from the urine of the patient. The vaccine is then injected intramuscularly at specific intervals to promote an antigen-antibody response and provide immunological information to the antibodies. The immunological response that results from the injection provides an enhanced specific cancer fighting mechanism.

Tumor substances are typically released into the blood and can be measured as a marker for malignancy. Some solid tumors or tissue bound tumors are the exception. They must be measured by biopsy. Generally, as tumors grow their secretions leak into the bloodstream or other fluids such as urine, stool, or tissue. Tumor markers include AFP, beta-HCG, CA 15-3, CA 19-9, CA 27-29, CA125, CEA and PSA. No tumor markers are completely accurate and can be found in non neoplastic conditions as well.

A study investigating the effects of AARSOTA found that B cell interaction with antigens that are immobilized on the surface of a target cell leads to the formation of a synapse and the acquisition, even of membrane-integral antigens from the target. The B cell antigen receptor accumulates at the synapse, segregated from the CD45 coreceptor which is excluded from the synapse, and there is a corresponding polarization of cytoplasmic effectors in the B cell.

The B cell antigen receptor mediates the gathering of the antigen into the synapse and its subsequent acquisition, thereby potentiating antigen processing and presentation to T cells with high efficacy. Synapse formation and antigen acquisition will probably enhance the activation of B cells at low antigen concentration and allow context-dependent antigen recognition and enhance the linking of B and T cell epitomes (Batista et al. 2001).

AARSOTA is an immunotherapy based on adoptive transfer of naturally occurring or gene-engineered T cells which can mediate tumor regression in metastatic cancer.

An investigation into the adoptive transfer of T cells focused on specific tumor cell eradication has found that more accurate targeting of antigens expressed by tumors is the key. The antigens and the associated vasculature of the tumor are significant in the use of gene engineered re-targeting of T cells before they are re-introduced into the patient. Further inquiry will lead to more effective promotion of tumor eradication (Restifo et al. 2012).

The AARSOTA Biological Vaccine has its historical roots in the research and methodology of Gaston Naessans Anablast vaccine from 1949. Today, this type of treatment is mainly done in Mexico by Dr. Rashid Buttar and Dr. Tony Jiminez at the Hope 4 Cancer Institute (see Fresh Cell Therapy and Dendritic Cell Vaccine).

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ACER NIKOENSE (NIKKO MAPLE)

Acer nikoense or Acer maximowiczianum (as more recently classified) is from the Canadian maple tree family and is known as Nikko maple. It was first introduced for cultivation worldwide in 1881, when seeds were imported by the Veitch Nursery in England after being discovered by Charles Maries in the forests of Hokkaido, Japan. It was originally grown for its medicinal uses including treatment for liver disease and acute and chronic eye disease at the Buddhist temple Tsubosaka Ders over 400 years ago. It is also widely distributed in regions of China.

Before isolated constituents of the Nikko maple were discovered, hot water extraction of the Acer nikoense showed concentration-dependent inhibitory effects of three variations of leukemia (P388) cells. The three variations are mouse leukemia P388, Doxorubicin-resistant P 338 and leczyme (catalylic lectin)-resistant P 388 cells. All cell lines had DNA fragmentation and morphological changes, condensed fragmented nuclei and increased expression of sialylated glycoconjugates on the apoptotic cells. This early study demonstrates apoptotic cell death in vitro of leukemia (P388) cancer cells by Acer nikoense (Ogawa et al. 1999).

A later study identified two active constituents; geraniin, and corilagin from Acer nikoense or (megusurino-ki) in Japanese. The IC 50 values for TNF-alpha release inhibition were 43microM for geraniin and 76microM for corilagin (Fujiki et al. 2003). Acer nikoense has other compounds including acerogenin-M which is a cyclic diarylheptanoid classified as a linear curcuminoid.

Other maple bark phenolics have been examined for their cytotoxic effects against human colon tumorigenic (HCT-116, HT-29, Caco-2) and non tumorigenic (CCD-18Co) cells. A standardized isolate ginnalin-A was used in the study. Ginnalin-A exhibited an IC50=35 and 16µg/ml with growth inhibition of two fold over the normal CCD-18Co cells. Ginnalin-A did not show any cytotoxic or apoptotic activity toward colon tumorigenic cell lines. The antiproliferative effects were revealed to be mediated through cell cycle arrest in the S-phase. Results suggest maple bark extracts could play a preventative role in colon carcinogenesis (Gonzalez-Sarrias et al. 2012).

The isolate corilagen from Acer nikoense is also found in Phyllanthus niruri (see Phyllanthus). Corilagin is a type of tannin with anti-inflammatory and antitumorigenic potential. Corilagin was recently tested against human ovarian (SKOv3ip and H08910PM), highly metastatic, and a non malignant ovarian (OSE) cells in a xenograft model. Results showed corilagin arrested ovarian cancer cells in the G2/M phase, inhibited TNF-α, inhibited TGF-β, and blocked canonical Smed and non canonical ERK/Akt pathways. The study demonstrates that corilagin is an effective therapeutic agent against the growth of ovarian cancer cells (Jia et al. 2013).

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ACORUS CALAMUS (CALAMUS/SWEET FLAG)

Acorus calamus or sweet flag is an aquatic plant that grows in ponds and lakes and the banks of quiet waters. The roots are gathered in early spring or late autumn. The roots stimulate sluggish digestive systems and give an overall strengthening affect to the body. Calamus is known to dissipate mucous and aid in quitting smoking. Acorus calamus has had a long history in indigenous medicine in Asia, Australia, Europe and North America.

Calamus root tea improves appetite and helps in kidney disorders. Many folk lore stories tell of this herb curing or helping in cancer and reversing the wasting stages. There are claims of cancer curing effects when combined with yarrow.

Acorus calamus rhizomes obtained from its natural habitat in the Coimbatore region, Tamil Nadu, India were used in an investigation for cytotoxic and antiproliferative activity using aqueous and methanolic extracts. The cell lines of human breast carcinoma (MBA-MB-435S) and human liver carcinoma (Hep3B) were used. Results showed the methanolic extract has significantly greater cytotoxic activity with IC50 of 13.71 ± 6.66µg/ml for MDA-MB-435S and 32.74 ± 4.55µg/ml for Hep3B cancer cell lines. This study demonstrates that a crude extract of Acorus calamus has strong anticancer effects and is a potential source of metabolites (Rajkumar et al. 2009).

A methanol extraction of Acorus calamus has recently been evaluated for cytotoxicity against breast carcinoma (MCF-7) cells and assessed by MIT assay. Several mechanisms of actions against the MCF-7 cells were detected. Growth inhibition was found in a dose dependent manner and the 50% cytotoxic effect (IC50) was found at 52.07µg/ml. This study used different concentrations of 18.75, 37.5, 75, 150 and 300µg/ml. The Acorus calamus extract showed a significant decrease in growth rate with a low concentration (less than 100µg/ml) of IC50 value compared to control and concluded that Acorus calamus can cause cell death to MCF-7 cancer cells (Sreejaya et al. 2013).

The most recent study of the cytotoxic effects of calamus has resulted in isolating a new steroidal glycoside, callaphylloside. The structure of the new compound was elucidated by spectral data analysis and chemical transformations. Spirsostanol and a-L-rhamnospyranosyl are linked to the C-2 of the inner glycopyranosyl molecular chain. Both compounds play a critical role in the effects of vincristine and vinblastine. There was further validation of the isolates; vincristine and vinblastine against four cell lines (Prawat et al. 2016). (see Catharanthus Roseus).

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AGARICUS BLAZEI MURRILL (ABM MUSHROOM)

Agaricus blazei Murrill (ABM) is a mushroom originally from Sao Paolo, Brazil. ABM has been traditionally used in local medicine and as a food source for centuries. It is known in Brazil as Cogumelo do sol or Medicinel. ABM was discovered by Japanese researcher Takatoshi Furumoto in 1960 and identified as ABM by Belgian botanist P. Heinemann in 1967. Traditional Brazilian Medicine has used it for a wide variety of illnesses. It is believed that it helps against physical and emotional stress, reduces cholesterol, immune activator, digestive disorders, circulatory disorders, prevention of osteoporosis, anti-ulcer, antidiabetic and anticancer.

In recent years, ABM has been under scrutiny in studies for anticancer activity. It has been used in Asian counties as an edible anticancer food. ABM is composed of 90% water, 2-40% protein, 2-8% fat, 1-55% carbohydrates, 3-32% fiber, and 8-10% ash and contains the highest amount of beta-glucans of any mushroom. Known as the "Mushroom of God"- studies in Japan and England have found ABM stimulates production of interferon and interleukin that indirectly function, destroy and prevent proliferation of cancer cells. ABM stimulates T lymphocytes and T helper cells.

Active anticancer compounds are attributed to fraction F111-2b which is composed of (1-6) B-D-gluco-pyranosyl. Different stages of, maturity of ABM can affect the potency of the α-glucans and β-glucans. In Japan there is an injectable form of ABM that demonstrates a 90% elimination of tumors in mice. The F111-2b polysaccharide protein complex was referred to in a study as an antitumor organic substance MIE (ATOM). It was tested against mouse sarcoma 180, Ehrlich ascites carcinoma, Shionogi carcinoma 42 and Meth A fibrosarcoma models and found to have significant antitumor activity (Ito et al. 1997).

AGARICUS PHALLOIDES D4

Agaricus Phalloides D4 (APD4) is a vaccine made from the Agaricus mushroom with a four times greater potency. This prescription is based on work by Dr. Fricker in Germany who is a cancer therapist. His observations are that the D4 or 4x potency has been successful in treating all kinds of cancer. The APD4 extract of an Agaricus mushroom is recommended not be taken in a lower dilution or in a higher concentration it must be 4x only.

Dosage:
Five drops twice a day initially
Gradually increase up to 15 drops
The highest possible dosage is 15 drops

AHCC

AHCC is an Active Hexose Correlated Compound derived from the ABM mushroom. It is widely used in Japan. It is especially good for avoiding secondary infections associated with cancer as well as abnormal cell prevention.

Active hexose correlated compound or AHCC, is a proprietary medicinal mushroom extract made from the Basidiomycete mushroom. Other mushrooms from this family of mushroom such as shiitake have been used in Japan and China along with conventional chemotherapy to reduce side effects and enhance efficacy of orthodox treatments.

Although more studies are needed, existing studies have demonstrated that AHCC can enhance natural killer cell activity to defend against cancer. Studies conducted by Sloan Kettering have demonstrated that chemotherapy weakened immune systems in mice but had greater recovery in immunity and antioxidant effects when administered AHCC.

In Japan, AHCC is the second most popular complementary and alternative medicine used by cancer patients with Agaricus blazei being the most popular by a ratio of 7:1. So far, AHCC is mostly recommended as an adjuvant to conventional cancer therapy. Most of the research on AHCC is by independent laboratories funded by manufacturers.

The preliminary studies have demonstrated that AHCC helps to increase production of specific cytokines such as interferon which can enhance NK cell activity. AHCC also increases tumor necrosis factor (TNF) which triggers apoptosis. In addition, AHCC stimulates interleukin 2 and 12 (IL2/IL12) which suppresses production of tumor growth factor (TGF).

Early studies from the 1990's demonstrated that AHCC could reduce tumors by 20% more than with chemotherapy alone and decrease metastasis by an additional 30% over just using chemotherapy (Ghoneum et al. 1994, 1995).

An investigation into the efficacy of AHCC found it improved prognosis of hepatocellular carcinoma patients following surgical treatment. The study was performed on 44 patients with histologically confirmed liver cancer. Survival time, Quality of life (QOL), immunological parameters related to liver function, cellular immunity and patient status were determined. Of the 44 patients, 34 received AHCC and 10 received placebo (control group). Patients in the AHCC treated group had a significantly prolonged survival (95%) compared to the control group. Quality of life, mental stability, and ability to have normal activities improved after 3 months of AHCC, using the Wilcox signed-rank test (on one sided test, p=0.028, 0.037, and 0.040) respectively. AHCC treated patients had longer survival times and had more stable AST and ALT levels as well as slight increases in IL-12 and neopterin (Cowawintaweewat et al. 2006).

AHCC not only is a strong immunomodulator, it has demonstrated effects as a chemo-potentiator. In a study on 22 tumor bearing mice (murine hepatoma H22), AHCC significantly enhanced the antitumor effects of low dose 5-fluorouracil (5-FU). The combination up-regulated the expression of Bcl-2 associated X protein (BAX) while down-regulated the expression of B cell lymphoma 2 (Bcl-2). These results suggest AHCC is beneficial for patients receiving chemotherapy (Cao et al. 2015).

A recent study examined the effects of AHCC with unresectable pancreas ductal adenocarcinoma (PDAC) patients receiving Gemcitabine chemotherapy. The patients were divided into 2 groups according to (AHCC group) intake or not (control group). C-reactive protein CRP elevation and albumin decline of AHCC group was significantly suppressed compared to the control group. Patients in the AHCC group had less frequency of taste disorders caused by the Gemcitabine treatment. There was also a 14% less adverse events contributing to a higher QOL in the AHCC group (Yanaqimoto et al. 2016).

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BLOOD TYPE CANCER DIET

The Blood Type cancer diet was developed by Dr. Peter J. D'Adamo utilising the antigen-antibody dynamic as well as individual blood type predispositions for a personalised dietary approach to cancer prevention and inhibition. A super beneficial category has been introduced with emphasis on cancer fighting foods for each blood type.

D'Adamo sees carcinogenesis as a two step process with an initial exposure, and a subsequent stimulation by some sort of promoter. Following exposure to a subcarcinogenic dose of a carcinogen (the initiator) the latent period can be shortened and the tumor yield increased by treatment with certain "promoting agents" (such as hydrocarbons) which may be mildly carcinogenic in initiator-stimulated tissue; a process that may be necessary to "lock in" the effect of the initiator. This has been postulated, because wound healing also has a tumor promoting effect: Wounding of an area of skin treated with a carcinogen brings out tumors along the edge of the wound (D'Adamo).

There are many factors that determine the initial phase of carcinogenesis. These include; age, sex, chemical/ environmental, chemical exposures, oncovirus exposure and oncogenetic predispositions and blood type.

The blood type factor in association with cancer is based mainly on statistical analysis showing trends from many test studies. "General patterns have emerged from numerous statistics on malignancy, coagulation and infection. Some of the findings on microbe receptors, and the association with important immune proteins are most convincing and suggest that blood group antigens do play an important biological role. A role that is often completely unrelated to the red blood cell. It can be said at the outset, that cancers in general tend to be associated with blood group A, and slightly less strongly with blood group B." (D'Adamo).

Research has found that specific blood types have greater or less defense against specific types of cancer. Below is a list of different types of cancer and how they pertain to blood types.

BLADDER CANCER

In bladder cancer, blood group A has the advantage with less likelihood of bladder cancer tumors and a higher survival rate. Blood group O's are more likely to have higher grade cancer and higher mortality rates. Blood type AB inherits the tendency for protection of bladder cancer from the A, but is compromised by having the B type, which has characteristics similar to that of blood type O.

BONE CANCER

The highest association of bone cancer disorders is with blood group B and a weaker association with blood group A. Blood group A's have a higher association with leukemia especially with subgroup A2's. Blood group O's have the highest resistance especially with blood group O females and patients with acute leukemia.

BRAIN & NERVOUS SYSTEM CANCER

Brain and nervous system type cancers are clearly more common with blood group A's. A weaker association of these types of cancer exists with blood group B. Blood group O is the most protected.

BREAST CANCER

According to D'Adamo, blood group A women are over represented among breast cancer patients and are more likely to have worse outcomes. Blood Group O has less likelihood of breast cancer and a slight higher degree of resistance and a significant lower risk of death.

Type AB's were more similar to blood group A's with increased susceptibility and more dramatic trends to re-occurrence and shorter survival.

Type B's tend to be more similar to type O's however if there is a family predisposition blood type B's could have a higher likelihood. Blood type B's also have a higher degree of re-occurrence if they develop breast cancer.

COLON CANCER

In this type of cancer, the most commonly recognized indicator is an altered blood group antigen expression. For instance, a person who is expressing an antigen that is incompatible with the individuals blood type such as a blood group B with an A antigen. The A antigen, blood group A's are the most vulnerable to colon cancer but not to the degree of that of stomach cancer.

The altered antigen expression can also happen with blood group O, B or AB expressing an A, B, H and Le(b) antigen that is not normally consistent with a persons blood type.

Colon cancer also depends to a large extent by other factors such as ones Rh factor. Although both Rh+ and Rh- individuals are both fairly close in ability to develop colon cancer. An Rh- is more likely to develop a localized tumor where as an Rh+ is prone to metastatic processes.

Other factors such as physical activity, high fat or low fibre diet, and exposure to chemicals, preservatives and sugar can also play a role. Although the A antigen link on the surface of tumors is not absolute, what is consistent is that derangement of blood type antigens is associated with tumors. The A antigen is the most common derangement.

CALCIUM D-GLUCARATE

Calcium D-glucarate is a calcium salt found in many fruits and vegetables such as grapefruits, apples, broccoli, cabbage, alfalfa, brussel sprouts and lettuce.

Oral supplementation of calcium-D-glucarate has been shown to inhibit beta-glucuronidase, an enzyme produced by colonic microflora and involved in Phase II liver detoxification. When beta-glucuronidase is produced by E. coli bacteria in the gut its action is to break the bonds between hormone compounds that the body is attempting to eliminate. When beta-glucuronidase breaks the bond, the toxin or hormone is again released into the body instead of being eliminated.

High levels of beta-glucuronidase are particularly associated with hormone driven cancers such as breast, prostate, colon and even lung cancer. Calcium D-glucarate has demonstrated an ability to neutralize glucuronidase and help strengthen the bonds between glucuronic acid and the cancer causing hormone or toxin being flushed from the body. The body is then able to rid the various toxic chemicals and hormones that could potentially activate tumor formation. During Phase II detoxification, chemical carcinogens, steroid hormones, and other lipid-soluble toxins are conjugated with glucuronic acid in the liver (glucuronidation), and excreted through the biliary tract. Beta-glucuronidase is capable of deconjugating these potential toxins, making it possible for them to be reabsorbed rather than excreted. D-glucaro-1, 4- lactone is the metabolite that has been shown to inhibit beta-glucuronidase activity, increasing excretion of conjugated xenobiotic compounds and decreasing activity of harmful substances that are most active in their deconjugated state (Walaszeck et al. 1988).

Therefore calcium D-glucarate is often used as a cancer preventative along with probiotics which help to reduce the number of beta-glucuronidase producing bacteria in the digestive tract. Clinical applications of oral calcium-D-glucarate other than regulation of estrogen metabolism, includes use as a lipid lowering agent (Altern Med Rec 2002).

Most of the original studies with calcium D-glucarate are attributed to Walaszeck (1986) who found that by giving calcium D-glucarate orally to animals gave a 5 hour effect. The carcinogenic compounds normally bound to DNA were reduced. In 1990 Walaszeck published an article showing that calcium D-glucarate lead to a decrease in the proliferation of tumors. Further articles where published in 1991, 1992, and 1993 testing calcium D-glucarate along with retinoic acid (derived from vitamin A) demonstrating increased antitumor activity. However, calcium D-glucarate is still able to have antitumor effects on human cancer cell lines when taken alone (Walaszeck et al. 1994).

Based on results of early studies Walaszeck found that calcium D-glucarate supplementation of 100mg will inhibit beta-glucuronidase for a maximum of 5 hours. However revised recommended dosages of calcium D-glucarate is between 400-600mgs daily split into two dosages as a preventative. Higher doses of 1000- 2000mgs are recommended for anyone with breast, prostate or other cancers.

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CAMELLIA SINENSIS (GREEN TEA)

Camellia sinensis is a shrub grown to make tea from its leaves. It has been used for its health and stimulant properties for nearly 5,000 years in China. Black tea which was thought to be from a different species is in fact fermented green tea. It is suggested that green tea has been used for as many as 200 illnesses. Camellia sinensis was introduced into Japan in around 600 AD by Buddhist priests. It spread to courtly and monastic circles during the 8th and 9th centuries and later was adopted by Japanese social classes who have drank it since.

Camellia sinensis or green tea contains the polyphenolic (-) epigallocatechin -3- gallate (EGCG), (-) -epicatechin -3- gallate (ECG), and (-)- epicatechin (EC), catechin, gallocatechin, epigallocatechin digallate, epicatechin digallate, 3-0-methyl EC and EGC, catechins gallate (CG), and gallocatechin gallate, all within similar quantities. EGCG has an antioxidant level between 25-100 times that of vitamin C and E and is the most potent in anticancer effects.

Extracts of green tea have been shown to have a cytotoxic shielding effect on cells due to its unique polyphenol, epigallocatechin gallate (EGCG). In a study against human prostate (PCa) cancer cells the ECGC isolate from green tea demonstrated an antiandrogenic effect. The green tea epigallocatechin-3 gallate (EGCG) and epigallocatechin (EGC) displayed strong growth inhibitory effects against lung (H661) and (H1299) with IC50 of 22 microM but less effective against the lung (H441) cancer cell line and colon (HT-29) cancer cell line with IC50 values 2-3 fold higher. Epicatechin-3 gallate had lower activities and (-)-epicatechin was even less effective (Yang et al. 1998).

A novel study was conducted using green tea extract combined with soy against human prostate cancer (LNCaP) cells implanted into mice. It was found that there was an inhibition of tumor growth and inhibition of MMP-9 and VEGF secretion and mitosis. In the study using soy and green tea derivatives there was a synergistic effect of inhibition of tumor progression in androgen sensitive (PCa) and dihydrotestosterone (DHT) concentration, while green tea alone inhibited tumor progression but elevated dihydrotestosterone (DHT). It was the combination of green tea and soy that inhibited tumor progression and tumor angiogenesis (Zhou et al. 2003).

ECGC has demonstrated the potential for reverse epigenetic changes by improving high-density lipoprotein and glucose homeostasis in overweight women who have had breast cancer (Stendell-Hollis et al. 2010). ECGC also inhibits the expression of fatty acid synthase in human breast (MCF-7) and human breast (AU 565) cancer cells by blocking heregulin through inhibition of phosphatidylinositol 3-kinase/Akt and mitogen activated protein kinase cascade signalling (Pan et al. 2007). The polyphenol ECGC inhibited human prostate carcinoma through inhibition of AR-dependent transcription in PCa cells (Siddiqui et al. 2008).

An investigation of pancreatic carcinoma shows that the antiproliferative action of EGCG was found to be meditated through programmed cell death or apoptosis as evident from nuclear condensation, caspase-3 activation and poly-ADP ribose polymerase (PARP) cleavage. EGCG-induced apoptosis of pancreatic cancer cells is accompanied by growth arrest at an earlier phase of the cell cycle epigallocatechin-3-gallate induces mitochondrial membrane depolarisation and caspase dependent apoptosis in pancreatic cancer cells. This was further elucidated by finding that ECGC inhibits epithelial-mesenchymal transition by upregulating the expression of E-cadherin and inhibiting the expression of N-cadherin and Zeb1. These findings indicate ECGC inhibits pancreatic cancer orthotopic tumor growth, angiogenesis, and metastasis which are associated with P13K/Akt and ERK pathways and activation of FKHRL1/FOXO3a (Shankar et al. 2012).

In an ovarian cancer study EGCG has demonstrated a repression of NF-kB and inhibition of proinflammatory cytokines such as TNF-α and IL-6 as well as stabilization of p53 protein and sensitization of TRAIL (TNF receptor apoptosis inducing lignand) inducing apoptosis in ovarian CSC's (Chen et al. 2012).

EGCG has demonstrated a novel dual effect on VEGF expression causing a secondary reactivation of apoptosis according to a study on human triple negative breast (Hs578T) cancer cells. After a 24h of 10 microM of EGCG treatment the inhibition of proliferation peaks then decreases at 48 and 72 hours. After 72h a reactivation of apoptosis occurred (Braicu et al. 2013).

Human colorectal cancer cell studies have received significant attention in investigations using EGCG. The study used 5, 10 and 20mg/kg of EGCG with (Lovo and SW480) cancer cells in vivo. Marked apoptosis was observed with the expressions of HES1 and Notch2 in EGCG treated groups which were remarkably lower than control (Jin et al. 2013). Human colorectal (HCT-116 and HT-29) cancer cells were treated with EGCG in an inquiry concerning morphological and proliferative changes that might occur. The study found that EGCG dose-dependently suppressed the proliferation of the HCT-116 and HT-29 cells and induced apoptosis via both p-53 dependent and p-53 independent pathways (Park et al. 2013).

In China a recent inquiry looked at the relationship of green tea consumption and stomach cancer incidence. The survey used 160 cases and 320 control subjects. A questionnaire was given to assess the green tea drinking habits of patients. The results found that green tea had a protective effect against the risk of stomach cancer. Efficacy was dependent on consumption rates with lower temperature tea yielding the best protective effects (Wang et al. 2015).

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CAMPHORIC CHLORIDE-(714X-TRIMETHYLBICYCLONITRAMINEOHEPTANE)

The 714X treatment was developed by researcher and biologist Gaston Naessens in the 1970's. Camphor is said to kill cancer cells and fungus especially when combined with nitrogen which attracts the cancer as in the 714X treatment. Some studies indicate positive results in lymphomas and melanoma.

714X is categorised as an immune-modulator health product aiming to both support a weak immune system or to slow down an over active one. It tends to restore the body's immune defenses without side effects.

714X is manufactured in Canada by the laboratory CERB Inc. and has been exported to over 80 countries since the mid 1990's. 714X is a colourless liquid. Its therapeutic mode of action requires that it is introduced via injection into lymphatic circulation (first treatment). In some cases, 714X can be introduced via the respiratory tract using a nebulizer (second treatment).

714X works in two ways:

1. In liquefying the lymph, 714X promotes cleansing for a better disposal of metabolic waste circulating in the blood (toxins).
2. Once 714X has been absorbed through the lymph, it brings to the blood circulation particular elements (structured and organised molecules including nitrogen fixed to camphor) to directly address white blood cells (leucocytes) to resume previously disrupted intercellular and extracellular communication.

The second function of 714X, by activating cytokine receptors specific to each group of white blood cells, assures a harmonious recovery of all immune defense levels.

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CONVOLVULUS ARVENSIS (BINDWEED)

Bindweed is from the species Convolvulaceae which is the morning glory family. This includes 1600 different varieties of what are considered weeds. Ironically it is often referred to as the "cancer of weeds" due to its highly proliferative nature. It characteristically wraps itself around crops such as corn and wheat and depletes the nutrients to those plants. Bindweed grows all over the world from Europe to China and from Canada to South America.

Bindweed contains an isolate, proteoglycan which in recent years has come under investigation for its antiangiogenic, immunostimulatory and antineoplastic activity. Claims are that proteoglycan (PGM) has over 100 times the antiangiogenic properties of shark cartilage. This makes (PGM) a strong anti-tumor/antiproliferative substance that inhibits and destroys the capillary vascular network from which cancer tumors use to feed.

Research studies demonstrating the extract of Convolvulus arvensis as a potential anticancer substance have used both human and mouse cells. In a mouse tumor model, the extract demonstrated antitumor effects in two different instances. The study concluded that the antiangiogenic mechanism of bindweed was not fully understood but it was definitely evident. The study showed a 54-77% inhibition by weight compared to controls, up to 96% by cellular composition. This was on mouse fibrosarcoma (S180) cells and Lewis lung carcinoma (C57) cells. In another study, a different substance, that has great potential to work in conjunction with PGM, was tested. Muramic acid a component of bacterial cell walls was tested along with PGM. Muramic acid has the ability to sensitize macrophages and other immunostimulatory factors. Muramyl peptides upregulates monocyte cytokine genes (IL-1beta,IL-6, IL-8, IL-12), macrophage chemotactic and activating factor, and tumor necrosis factor-alpha. Muramyl peptides did not increase (IL-2 or (IL-10) TNF or activate monocyte-mediated tumoricidal activity. Another demonstration of the cytotoxic effects β-elemene derived from Convolvulus myrrha showed an induction of apoptosis against human renal carcinoma (786-0) cancer cells through inhibition of MAPK/ERK and P13K/Akt/mTOR signalling pathways (Zhan et al. 2012).

The muramyl polysaccharide-glucan complex (MPGC) is a non toxic bacterial cell wall extract of Lactobacillus fermentum that contains muramic acid moieties attached to variable length mannose rich polysaccharides.

The MPGC appears to have a broader scope of application than PGC in that it has the same effect as an angiogenesis inhibitor but also a stronger effect on chronic infections and cells infected with oncogenic viruses. In a study with mouse sarcoma MPGC demonstrated inhibitory tumor effects and reduction of proliferation (Riordan et al. 2000).

Dr. Neil Riordan PhD from the center for Improvement of Human Functioning and Bio-Communications Research Institute in Wichita, Kansas is one of the researchers of bindweed extracts. He tested the combined PGM from Vascustatin and MPGC (muramyl polysaccharide-glycan complex, a non toxic purified extract of bacterial cell walls of gram-positive bacteria). The results in tumor regression at a dose of 1000mg per day of each showed significant tumor regression. "We have seen regressions of tumors in people using four to six capsules of each per day. It is likely that a greater response could be seen with higher doses. We use a maintenance dose of four capsules per day of both PGM and MPGC after patients start to respond. The fastest shrinkage we have seen in ten days in a liver metastasis from colon cancer".

There have been many individual case studies and testimonials from doctors that claim significant tumor regression in sarcoma type cancers and especially ovarian cancer. A recent study investigated the different properties of Convolvulus arvensis (PGM) including antitumor, antiangiogenic and immunostimulatory activities. The study found leishmicidal activity and significant antiangiogenic activity due to inhibition of vascular-like tubes of human umbilical vein endothelial cells (HUVEC) (Mahmoudi et al. 2014).

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COPTIS JAPONICA (HUANG LIAN)

Coptis japonica is known in China as Huang lian and is a popular traditional herbal remedy. There are 15 different species of coptis and like ginseng it takes on the qualities of the soil wherever is it grows around the world. It is mainly known in Chinese medicine for clearing heat and toxicity. It has been used for a wide variety of conditions including bacterial, viral, fungal, parasites, heliocobacter pylori and skin acne. Coptis is well known for its antibiotic effects and for helping in cases of hypertension, hyper- glycemia and hypercholesterolemia.

Coptis's main constituent therapeutic ingredients are isoquinoline and berberine. In coptis, berberine exists mainly in its natural state as piotoberberine. Studies have demonstrated that berberine is the main antitumor and antiproliferative component. Coptis and berberine have demonstrated apoptosis in a variety of cancer cells. It inhibited tumor growth in MGC-03 stomach cancer cells with reports of apoptosis of human promyelocytic leukemia (HL-60) and murine myelomonocytic leukemia (WEHI-3) cells (Lin et al. 2006).

In a study conducted in 2005 using human gastric cancer cells (SNU-668), Coptis japonica demonstrated a significant apoptotic effect through various pathways. Coptis diminished BCL2 expression while increasing BAX and caspase-3 expression, compared to control. The caspase-3 activation is the main inducer of apoptosis on human gastric (SNU-668) cancer cells (Park et al. 2005).

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DRACAENA SPECIES (DRAGONS BLOOD)

Dragons' blood from Daemonorops draco is a deep red resin which has been used in traditional medicine since ancient times. Dragons' blood was used by early Greeks, Romans and Arabs as a cure-all and wound healer. It has been used as a coagulant for curing diarrhoea, lowering fevers, mouth ulcers, eczema, intestinal and stomach soother and as an antiviral for stomach, respiratory viruses and gonorrhoea.

There are other species from which the sap or resin dragons' blood are derived including; Daemonorops spp., Dracaena arbosa, Dracaena cambodiana, Dracaena cinnavari, Draceana cochinchinensis, Draceana draco, Dracaena fragrans, Dracaena loureiri, Dracaena manni, Dracaena mariginata, Dracaena sanderiana, Dracaena tamaranae, Pterocarpus officinalis. Since dragons' blood, as a name, has been applied to resins obtained from different species there is a great need to identify them apart.

Purified compounds from various species of dragons' blood may vary in quantity and quality. Steroidal saponins from different species have demonstrated cytotoxic activities. The steroidal saponins draconin A and draconin B from the bark of Dracaena draco demonstrated apoptotic hallmarks against human leukemia (HL-60) cells (Gonzeley et al. 2004) and the saponin isogenin also inhibited growth of HL-60 by induction of apoptosis with the isolate dioscin displaying similar activity as icogenin (Hernandez et al. 2004). A cytotoxic research study was performed using a homoisoflavonoid isolate known as cambodianol derived from Dracaena cambodiana. Cambodianol was tested against two different human cancer cell lines; myelogenous leukemia (K562) and gastric (SGC-7901). Cambodianol exhibited an IC50 value of 1.4 and 2.9µg/ml respectively (Liu et al. 2012).

Investigations of cytotoxic compounds from dragons blood has led to a new synthetically produced analogue known as dracorhodin perchlorate (DP).

Previous investigations have shown apoptotic effects on human leukemia (HL-60) cells with DP (Xia et al. 2006) as well as with human melanoma (A375-S2) cells where DP activated caspase activity via p53 pathway (Xia et al. 2005).

DP has been found to inhibit P13K/Akt and NF-kB activation while upregulating p-53 expression in a study against human prostate (PC-3) cells. This study demonstrated DP to induce antiproliferative and apoptotic effects (He et al. 2011).

Dracorhodin perclorate has also demonstrated apoptosis in human breast cancer (MCF-7) cells through a non caspase -3 dependent or caspase independent pathway. DP induced apoptosis in MCF-7 cells through the mechanism of the mitochondrial membrane potential (MMP) and increased expression of Bax while decreasing the expression of Bcl-2. This investigation also revealed that DP releases cytochrome C to promote the activation of caspase-9. This study suggests DP could be useful in treatment of human breast cancer (MCF-7) (Yu et al. 2013).

The effects of DP have not been reported in relation to cytotoxic effects against human lung squamous carcinoma (SK-MES-1) cells. A recent study has investigated any potential antitumor mechanisms DP might promote on cell viability. The study in question found DP produced DNA morphological changes inhibiting the growth of SK-MES-1 cells by inducing apoptosis and G1/G0 cell cycle arrest (dose dependent) via activation of p-53. DP also upregulated B cell lymphoma -2 (Bcl-2) activated X protein and significantly downregulated Bcl-2, inducing dissipation of mitochondrial membrane potential (MMP). Unlike other studies with DP, this study found activation of caspase-3 by cleavage of (PARP) to induce caspase dependent apoptosis as well as a significant increase in reactive oxygen species (ROS). This study demonstrates DP to induce apoptosis in human lung SK-MES-1 cells through caspase induced and mitochondrial membrane pathways (Zhang et al. 2015).

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EBC-46

EBC-46 is a cytotoxic phenolic compound extract from the seeds of the blushwood tree. The blushwood tree grows beneath the forest canopy top at a height of 15 meters where it avoids direct sunlight. The tree is from the Fontainea family including Fontainea picrosperma/Hylandia dockrillii, and Fontainea venosa.

When injected into a tumor or applied by gel, EBC-46 activates a local tissue response through the protein kinase C (PKC) pathway producing an antiangiogenic effect that cuts the blood supply to the tumor.

INDIGO NATURALIS (QING DAI)

Indigo naturalis or Qing dai has been used in traditional Asian botanic medicine for centuries for external and internal healing applications. In China, Korea, India and Thailand Indigo naturalis is used for topical skin conditions such as eczema and psoriasis. As an internal medicine Indigo naturalis has a wide variety of uses.

One of its constituents; isorhamnetin (see Isorhamnetin) has demonstrated antiproliferative and apoptotic effects in a wide variety of cancer cell types. Isorhamnetin along with indurubin-3-monoxime and tryptanthrin are classified as CDK (cyclin-dependent kinase) inhibitors, which control cell division which explains why Indigo naturalis has been used predominantly for leukemia in China.

Qing dai containing indirubin has shown strong affects 70-80% in fighting prostate cancer with less effectiveness in granulo-leukemia 25%. Indirubin is also one of the key ingredients in the famous Chinese PC-SPES prostate cancer treatment. In addition to being a potent selective cyclin-dependent kinase (CDK) inhibitor, indirubin has cell permeable characteristics. It has been used in China for years for treatment of leukemia with a 26% total remission.

Indirubin-3-monoxime has been studied for its various apoptotic mechanisms in various cancers other than leukemia. These include bladder, oral/laryngeal, kidney, lung, colorectal and prostate. Test studies on indirubin number into the hundreds since the early 1990's on many varieties of human cancer cell lines. Renal cancer studies are the most recent. Indirubin has demonstrated cell growth inhibition, antiproliferative and various apoptotic mechanisms (Data et al. 2010).

In a lung cancer cell investigation indirubin-3-monoxime was tested in a study using human adenocarcinoma in xenograft mice. Results indicated a reduction in tumor and fragmented and condensed nuclei, implying apoptosis in (BPA) induced lung cancer (Ravichandran et al. 2010).

In human bladder (RT4, RT112, T24, TCC-SUP) cell lines treatment with indirubin-3-monoxine increased the expression of survivin almost four times in RT4 cells and more than doubled it in the RT112 and T24 cells. In SUP cells, the expression of survivin increased more than seven fold after 72h incubation. Once again indirubin demonstrates properties of being a potent selective inhibitor of cyclin dependent kinases (CDK) (Perabo et al. 2006)

Indirubin is found to promote autophagic and apoptotic death in human acute lymphoblastic leukemia (JM1) cells and chronic myelogenous leukemia (K562 cancer cells (Lee et al. 2013).

In human laryngeal cancer, indirubin was studied for its propensity for antiproliferative effects and apoptotic mechanisms in HEp-2 cells. Results demonstrated a 50% increase in antiproliferation (Paulkumar et al. 2010).

In a study with renal cancer, indirubin inhibited antiapoptotic HO-1 and promoted overexpression of CXCR3-B in human (CAK-1) cells. Indirubin further downregulated the expression of heme oxygenase-1 which mediated growth inhibition. This was further demonstrated in three human renal cancer cell lines (A498, CAK-1, CAK1-2) and one murine renal cell cancer (RENGA) (Perabo et al. 2011).

Scientific inquiry in human pancreatic (Panc-1, MIA-PaCa2, BxPC-3 and AsPC1) cancer cell found indirubin exhibited novel inhibitory responses. There was an inhibition of SRC family of kinases (SFKs) which leads to reactivation of signal transducer and activator of transcript 3 (STAT3) and tumor cell survival through downstream STAT3 signalling (Nam et al. 2013).

Recently Indigo naturalis and another one of its components, tryptanthrin have been confirmed to inhibit in vivo vascular endothelial growth factor (VEGF) which induces angiogenesis. Tryptanthrin demonstrated cell cycle arrest and dose-dependently decreased the expression of cyclin A, cyclin B, cyclin dependent kinase (CDK) 1 and 2 but not cyclin D or cyclin E, at both the MRNA and protein levels. This study showed that tryptanthrin can induce the phosphorylation of both protein kinase B (PKB or Akt) and focal adhesion kinase (FAK) (Chang et al. 2015).

Recently further validation of the three active components of Indigo naturalis; indirubin, tryptanthrin and isorhamnetin have been investigated and reviewed for their antileukemic effects. In particular isorhamnetin was found to target photo-oncogene constant (Kd). Isorhamnetin showed antileukemic effects on (K562) cells by inducing G2/m cell cycle arrest (Wu et al. 2016).

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MELATONIN

Melatonin (N-acetyl-5-melhoxytryptamine, MLT) is the main hormone produced by the pineal gland. Melatonin not only regulates circadian rhythm, but also has antiageing, antioxidant and immunomodulatory effects. It has significant antiproliferative effects against solid tumors along with apoptotic, oncostatic and antiangiogenetic properties.

One of the earliest studies on the effects of melatonin against malignant neoplasms dealt with breast cancer (MCF-7) cells. It was originally proposed that the pineal hormone melatonin with its antireproductive effects may also exert oncostatic effects that could inhibit mammary cancer growth. Melatonin was found to completely block the estradiol induced stimulation of MCF-7 cell proliferation. However in a serum free medium melatonin loses its anticancer effects unless directly exposed to estradiol or prolactin (Blask et al. 1986).

Studies have found induced disruption of the circadian nocturnal melatonin signal promotes growth, metabolism and signalling of human breast cancer and drives breast tumors to endocrine and chemotherapeutic resistance. In a xenograft model the anticancer mechanism of the circadian melatonin signal involves MT1 receptor-mediated expression. In estrogen positive (ERα) positive breast cancer, melatonin suppresses ERα MRA expression and ERα transcriptional activity via the MT1 receptor. Melatonin also suppresses tumor aerobic metabolism (Warburg effect) and cell signalling proliferative pathways that promote cell survival and metastatic mechanisms. Melatonin also possesses anti-invasive/antimetastatic actions that involve multiple pathways including inhibition of p38 MAPK and repression of epithelial-mesenchymal transition (EMT) while promoting genomic stability by inhibiting the expression of LINE-1 retrotransposons.

As elucidation of multi-mechanisms of melatonin become more apparent, the implications on elevated cancer risk in shift workers are of concern. A study investigating the higher possible risk of night shift workers found a correlation with incidence of colorectal cancer. Although studies have confirmed increased risk with lack of melatonin causing proliferative cancer risk in breast cancer, colorectal cancer had not been previously considered. The study into the effects of colorectal cancer incidence in nightshift workers documented 602 incident cases among 78,586 women (nurses) who were followed up from 1988 through to 1998. Compared to women who never worked rotating night shifts, women who worked 1-14 years or 15 years in night shifts of at least three nights per month had a higher risk of colorectal cancer (Schernhammer et al. 2003).

Melatonin has a free radical scavenging effect and dramatically lowers oxidative stress on neural mitochondria. Studies have shown it boosts T helper cells and stimulates the tumor killing action of natural killer (NK) cells by increasing the production of cytokine interleukin-2 (IL-2).

In an integrative study, 100 neoplastic patients were randomized to receive chemotherapy alone or chemotherapy and melatonin. The patients all had metastatic non small cell lung cancer and were assessed over a 5 year period. The results showed that no patients survived after two years who had chemotherapy alone. Of the 50 patients who had chemotherapy and melatonin; three of 47%, (6%) were still alive after 5 years. The mechanisms of melatonin for survival are prevention of chemotherapy induced lymphocyte damage and antioxidant effects that have been proven to enhance the cytotoxic effects of the chemotherapy (Cisplatin and Etoposide) (Lissoni et al. 2003).

By activation of its MT1 receptor melatonin can modulate the transcriptional activity of various nuclear receptors and proliferation of ERα+ and ERα- human breast. A study demonstrates how melatonin can significantly suppress the proliferation of both estrogen receptor alpha (ERα)-positive (MCF-7, T47D, ZR-75-1) cells and ERα - negative (MDA-MB-468) breast cancer cells in vitro. Melatonin however has no antiproliferative effect on ERα- negative breast (MDA-MB-231, MDA-MB-330, or BT-20) cancer cell lines. Other antiproliferative effects of melatonin have been shown in prostate (PC-3), ovarian (SKOV-3), endometrial (Hec 1A), liver (HepG2) and osteosarcoma (Sa0S-2) cancer cells (Hill et al. 2009).

A recent review of studies using melatonin in oncology has found that the well documented anticancer properties with an antitoxic, trophic, immunostimulating, differentiating, radioprotective and radiosensitizing effects. These properties make melatonin an underestimated pineal indole for use in oncology (Di Bella et al. 2013).

A study investigating the melatonin-mediated circadian regulation and integration of molecular signalling mechanisms involved in human breast cancer growth. In estrogen receptor-positive (ERα+) human breast cancer cells, melatonin suppresses both m RNA expression and estrogen- induced transcriptional activity of the ERα via MT_1 induced activation of Gai_2 signalling and reduction of c-AMP levels. The anti-invasive/antimetastatic actions of melatonin involve the blockade of p38 phosphorylation and matrix metalloproteinase expression. Melatonin suppression c-AMP leads to a blockade of linoleic acid uptake and its metabolism to the mitogenic signalling molecule 13-hydroxyoctadecadienoic acid (13-HODE). Downregulation of 13-HODE reduces activation of growth factor pathways supporting cell proliferation and survival (Hill et al. 2015).

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VITAMIN V (NAD/NADH)

Vitamin V is otherwise known as nicotinamide adenine dinucleotide (NAD) and nicotinamide adenine dinucleotide plus hydrogen makes NADH.

NAD is a co-enzyme found in every cell of the body and plays a critical role in the formation of energy and transfer reactions in living cells. Increased dosages of NAD caused an increase in synthesis of vital neurotransmitters in brain tissue. It is useful for healing depression, fatigue, Alzheimer's, Parkinson's and improving overall muscle stamina. Therefore it is a good adjunctive treatment in treating cancer because it utilises redox reactions in the body which involves multiple metabolic processes.

NADH increases cell energy production and keeps cells alive for a longer period of time. NADH plays an active role in correcting conditions that cause degenerative diseases. It has positive effects in immunostimulation activity and repair of damaged DNA.

An early investigation into the cellular defense of NAD/NADH against ATP depletion and cell death took place in a study from 1988. This study used human hepatocytes against cytotoxic menadone a (2-methyl-1, 4-naphthoquinone), dimethylsulphate and hydrogen peroxide in relation to their effects on intracellular NAD+ and ATP levels. Both dimethylsulphate and peroxide generated by glucose/glucose oxidase, caused depletion of NAD+. This reaction was due to an activation of poly (ADP-ribose) polymerase as it was prevented by inhibitors 3-aminobenzamide and nicotinamide.

The protection of intracellular NAD+ was accompanied by a prevention of the cytotoxicity of both dimethylsulphate and glucose/glucose oxidase, while it did not alter the decrease in intracellular ATP. This study is an early demonstration of the role of NAD in the maintenance of cellular integrity (Stubberfield et al. 1988).

A study examined inhibition of tumor progression in breast cancer by NAD and its reduced form NADH. As metastasis remains the leading cause of death in breast cancer patients, the effects on mitochondrial DNA mutations and oxidative phosphorylation are of importance (Chatterjee et al. 2006). NAD/NADH was shown to interfere with oncogene-driven breast cancer progression and increase survival time by actively inhibiting tumor growth through redox balancing (Santidrian et al. 2013).

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WITHANIA SOMNIFERA (ASHWAGANDA)

Withania somnifera is commonly known as ashwaganda, winter cherry, Indian ginseng and poison gooseberry. Withania somnifera is from the Solanaceae or nightshade family and has been used in Ayurvedic medicine for hundreds of years. It has been used for endocrine disorders and as a tonic to improve health and longevity and to prevent disease in athletes, elderly and during pregnancy. Withania somnifera has also been used for a variety of other ailments including arthritis, rheumatism, cardiopulmonary, immunomodulatory, nervous system disorders, and has antioxidant, antistress, and antitumor properties (Mishra et al. 2000).

In a study with urethane induced tumors in mice the protective effects of Withania somnifera have shown increased life span and decreased tumor weight and proliferation. This study also demonstrates a reversal of neutropenic side effects of chemotherapy by Withania somnifera (Gupta et al. 2001).

The pharmacological effects of root extractions of Withania somnifera are attributed to withanolides which have some similarities to ginenosides found in Panax ginseng. In particular withaferin A has been investigated in numerous studies for its cytotoxic and cancer inhibitory effects on its own and with conventional treatments. One study demonstrated withaferin A to be equal or greater to the drug Doxorubicin in its inhibitory effects against human breast, central nervous system, lung and colon cancer cell lines (Jayaprakasam et al. 2003). Withaferin A uses a reactive oxygen species (ROS) mediated pathway generating mitochondrial dysfunction and apoptosis in human leukemia (HL-60) cancer cells (Malik et al. 2007).

Research into metastatic processes in breast cancer has found that epigenetic alterations that transform stationary epithelial cells into migratory cells is a process termed epithelial-mesenchymal transition (EMT). EMT proteins are over expressed in highly invasive human tumors and with breast cancer in particular. The EMT known as vimentin has been reported as correlating with metastatic disease. A study investigating the vimentin over expression found that Withania somnifera extract directly binds vimentin and inhibits its assembly through a covalent modification of cysteine 328. The Withania extract withaferin A is the most abundant isolate inducing apoptosis in vimentin expressing tumor cells via phosphorylation confirming antimetastatic activity (Thaiparambil et al. 2011). Withaferin A has demonstrated apoptotic activity against a wide variety of cancer cell types including human breast (MDA-MB-231 and MCF-7) cancer cell lines (Hahm et al. 2011).

Withaferin A has also demonstrated an induced N-acetyl-L-cysteine repressible enhancement in cellular oxidative potential/stress with subsequent induction of a heat shock stress response in human glioblastoma. This response took place through HSP_{70}, HSP_{32} and HSP_{27} upregulation and HSF_1 downregulation. In addition withaferin A induced all dose-dependent G2/M cell cycle arrest and promoted cell death through extrinsic and intrinsic pathways. A further shift in the inhibition of the Akt/mTOR signalling pathway and diminishing of phosphorylation of Akt, mTOR, p7056K, and p856K with increased activation of AMKa and the tumor suppressor tuberin/TSC2. Other observations include an alteration of proteins of the MAPK pathway and cellular receptors; EGFR, HER2/ErbBz and c-Met making withaferin A a candidate for glioblastoma treatment (Grogan et al. 2013).

ANTICANCER SYNERGISTIC PLANT METABOLITES

The following are examples of an ever expanding field of research whereby endophytic cytotoxic/apoptotic metabolites are produced from the combining of two plant species.

CAJANUS CAJAN (PIGEON PEA)/HYPOCREA LIXII

Cajunus cajan or pigeon pea is a perennial legume from the Fabaceae family. It is believed to have originated in India 3,500 years ago and its seeds are used as food in Asia, Africa and Latin America for its high protein content.

Pigeon pea is now cultivated in more than 25 tropical and subtropical countries and mixed in cereals or used as a sole crop. India produces approx. 77% of the crop and it is used as an animal feed crop in Africa.

An isolated isoflavones from Cajanus cajan called cajanol has been identified as an anticancer agent. It has other properties including; antiplasmodial, antifungal, and antimicrobial. It has been found to be produced by the endophytic fungus Hypocrea lixii isolated from the roots of the host plant Cajanus cajan. The level of cytotoxic activity towards human lung carcinoma (A549) cell lines has been demonstrated and is greater for fungal-produced cajanol than normal plant produced cajanol.

Cajanol produced by endophytes were quantified by liquid chromatography-tandem mass spectrometry (LC-MS/MS). R-18 produced the highest levels of cajanol (322•4 ± 10•6μg l(-1) or 102•8 ± 6•9μg g(-1) dry weight of mycelium) after incubation for 7 days. The cytotoxicity towards human lung carcinoma cells (A549) of fungal cajanol was investigated in vitro.

Fungal cajanol possessed stronger cytotoxicity activity towards A549 cells in time- and dose-dependent manners. This endophyte is a potential handle for scientific and commercial exploitation, and it could provide a promising alternative approach for large-scale production of cajanol to satisfy new anticancer drug development (Zhao et al. 2013).

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COMBRETUM LEPROSUM/ASPERGILLUS ORYZAE

Combretum leprosum is a semi deciduous tree which can grow as a small tree or a climbing shrub. It is found in South America, Argentina, Paraguay, Brazil and Bolivia.

Combretum leprosum has many (as yet) unidentified compounds with anticancer activity. A recent study has found extracts of Combretum leprosum (ethanolic extract) can prevent motor and molecular changes and partially reverted dopamine deficit in Parkinsons disease (Moraes et al. 2016).

The recent increase in human diseases and cancers requires new drugs to combat them. Sources have been found in rare microorganisms, those from extreme habitats, and from endophytes. In this study, the biological activity of endophytic fungi associated with the Brazilian medicinal plant Combretum leprosum was assessed. Cytotoxic and antiproliferative effects were evaluated using seven human cancer cells lines cervical (HeLa), bladder (ECV304), melanoma (B16F10), histiocytic sarcoma (J744), leukemia (P388), leukemia (Jurkat) and leukemia (K562). In addition the minimum inhibitory concentration (MIC) against pathogenic human fungal was determined using four candida species and the filamentous fungi Cryptococcus neoformans and Trichophyton rubrum.

A compound from extracts of phylotype Aspergillus oryzae CFE108 exhibited the most significant cytotoxicity effect against histiocytic sarcoma (J774) (IC50 of 0.80μgmL−1), leukemia (Jurkat) (IC50 of 0.89μgmL−1), bladder carcinoma (ECV304) (IC50 of 3.08μgmL−1) and cervical cancer (HeLa) (IC50 of 2.97μgmL−1).

Extracts of the fungus Aspergillus oryzae CFE108 showed significant cytotoxic effects against cell lines resulting in histiocytic sarcoma (J774) with IC50 of 0.08 and leukemic T cell lymphoblast (Jurkat) with IC50 of 0.89. The greatest inhibition was against bladder carcinoma (ECV304) with IC50 of 3.08 and cervical cancer cell lines (HeLa) with IC50 of 2.97. (Santos et al. 2012).

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EPHEDRA FASCICULATA/FUSARIUM OXYPORUM

Ephedra fasciculata is a shrub from the Ephedraceae family that grows from 350m up to 1200m. Ephedra fasciculata is endemic to southwest USA occurring in the states of Arizona, California, Nevada and Utah.

Fusarium oxporum is an ascomycete fungus that is considered a genetically heterogenous polytypic morphospecies. This adaptable fungus has been found in soils ranging from the Sonoran Desert to tropical rainforests, grasslands and tundra.

GLOSSARY OF RELEVANT TERMS

AERODIGESTIVE TRACT is the combined organs and tissues of the respiratory tract and upper part of the digestive tract.

ALLELE is one of the possible forms of a gene. Most genes have two alleles, a dominant allele and a recessive allele. An organism is heterozygous for that trait, or possesses one of each allele. The dominant allele is expressed.

ASCITES is the accumulation of fluid in the peritoneal cavity, causing abdominal swelling. It usually occurs when the liver stops working properly.

ANGIOGENESIS is the physiological process through which new blood vessels or capillaries are formed in order to increase growth as in tumors.

ANOIKIS is a type of apoptosis that is induced by inadequate or inappropriate cell matrix interactions. It can be involved in a wide diversity of tissue-homeostatic, developmental and oncogenic processes.

ANTIANGIOGENESIS is the process by which blood vessels or capillaries are decreased in order to inhibit growth of a tumor

ANTIMUTAGENIC is the effect of an agent that interferes with the mutagenicity of a substance.

ANTIPYRETIC is a substance used to reduce fevers.

AMPHILPHILIC is a chemical compound possessing both hydrophilic (water soluble) and lipophilic (fat soluble) properties. Lipids are amphilphilic.

APOPTOSIS is when a cell commits suicide or something triggers the death of a cell. This happens by proteins called caspases which spur the production of enzymes known as DNAses which destroy the DNA in the nucleus of the cell.

AUTOHEMOTRANSFUSION is when blood is drawn from a patient then subjected to ozone and then reintroduced back into the patient.

AUTOPHAGY is a cell self-eating mechanism caused by a degradation of proteins outside of the proteolytic/proteasomal pathway by another source.

AUTOSCHIZIS is a type of cancer cell death whereby the cancer cell membrane is compromised causing the cell contents to leak out. This has been demonstrated in studies using vitamin K3 and vitamin C combined. (Previously known as atypical apoptosis).

BENIGN is a neutral state or non invasive non harmful state.

BIOAVAILABLE is the ability of a substance to be absorbed and be effective on cellular structures and metabolism.

CACHEXIA is the weakness and wasting of the body due to severe chronic illness.

CANCER is a disease of uncontrolled proliferation and growth of cells at inappropriate times and locations in the body and when cells acquire mutagenic stimuli that compromise normal cellular replication, the cells form masses called tumors. Under current reasoning, the cells can become malignant and potentially invade other tissues due to metastasis.

CARCINOGENESIS is the process of development of cancer.

CARCINOMA is a new growth or malignant tumor that occurs in epithelial tissue.

CHEMORESISTANCE is specific resistance by components in a cell to a chemical substance or the resistance of bacteria or a cancer cell to a chemical designed to treat the disorder.

CLEAVAGE is the ability of a signalling substance to lock on another protein resulting in the irreversible commitment to cell death. Such is the case with caspase substrates MEKKI, p21-activated kinase2, and focal adhesion kinase that form into cancer killing agents when cleaved.

CONTRAINDICATED is when a substance is not compatible with another or when one agent creates a side effect with an already established substance that is to the detriment of the host.

CYTOSTATIC is the inhibition or suppression of cellular growth and multiplication.

CYTOTOXICITY is the quality of being toxic to cells.

DEPHOSPHORILATION is the removal of a phosphate from an organic compound by hydrolysis. Dephosphorylation activates and deactivates enzymes by cleaving phosphoric esters and anhydrides. A notable occurrence of dephosphorylation is the conversion of ATP to ADP and inorganic phosphate.

HUMAN CANCER CELL TYPES & PRO-APOPTOTIC AGENTS

The following table is of Cancer Cell Types along with the corresponding cytotoxic botanical herb, isolate, lignin or natural compound found in human cell evidence based test studies. (Therefore not all therapies listed in this book are included in this table.)

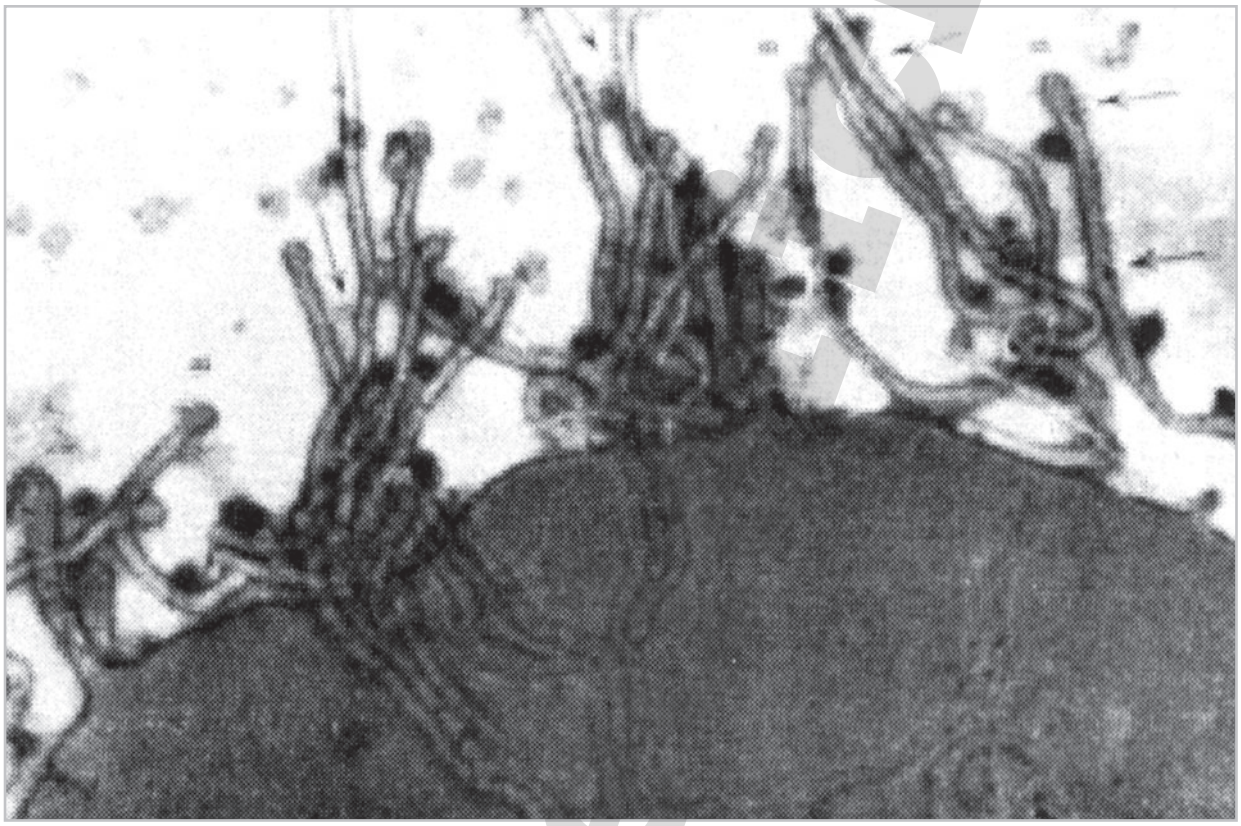
Cancer Cell Lines		Therapeutic Agent
ASCITES CARCINOMA		
ZR-75-1	Breast Ascites	Honokiol, Magnolia officinalis, Melatonin
BLADDER		
A637	Carcinoma	Petiveria alliacea
ECV-304	Carcinoma	Combretum leprosum/Aspergillus oryzae
J82	Transitional Carcinoma	Boswellia, Broccoli sprout, Lycopene
RT4	Carcinoma	Antrodia camphorata, Indirubin
RT112	Carcinoma	Indirubin
TCC-SUP	Grade IV Transitional Carcinoma	Indirubin
TSGH8301	Carcinoma	Antrodia camphorata, Ellagic acid
T24	Transitional Carcinoma	Aloe-Emodin, Antrodia camphorata, Broccoli sprout, Fucoidan, Geranium robertianum, Indirubin, Magnolia officinalis, Momordica charantia, Plantago major, Rosmarinus officinalis, Saussaurea lappa, Stephania tetrandra
BREAST		
AU 565	Adenocarcinoma	Camellia sinensis
BT-20	Carcinoma	Erythrophleum suaveolens
BT-474	Epithelial Carcinoma	Silybum marianum
BT-549	Carcinoma	Erythrophleum suaveolens, Nigella sativa, Sida acuta
EFM-19	Carcinoma	Cannabis indica
HBL-100	Carcinoma	Tanacetum parthenium
Hs578T	Fibroblast Carcinoma	Camellia sinensis, Laetrile, Scutellaria barbata
MCF-7	Adenocarcinoma	Acorus calamus, Aloe-Emodin, Antrodia camphorata, Arctium lappa, Artemisa annua, Artocarpus communis, Astragalus membranaceus, Beauvericin, Betanin, Bikaverin, Bidens pilosa, Boswellia, Calcium D-glucarate, Camellia sinensis, Cannabis indica, Cassia fistula, Castanospermum australe,Catalase, Cayaponia tayuya, Centella asiatica, Commiphora myrrha, Crocus sativus, Curcuma longa, Daidzein, DIM, Dracohodin perchlorate, Ephedra fasciculate/Fusarium oxyporum, Eugina jambolana, Eugenol, Evodia rutacarpa, Frondoside A, Fucoidan, Garcinia hanburyi, GcMAF, Genistein, Geranium robertianum, Glyceollin, Grifola frondosa, Himatanthus sucuuba, I3C, Inonotus obliquus, Iodine, Juglans nigra, Lactoferrin, Laetrile, Larrea tridentata, Lentinus edodes, Lithospermum erythrorhizon, Lycopene, Magnolia officinalis, Melatonin, Methyl jasmonate, Methylselenocysteine, Momordica charantia, Nigella sativa, Oridonin, Oryza sativa, Pfaffia paniculata, Phyllanthus niruri, Plantago major, Punica granatum, Rabdosia rubescens, Reserpine, Resveratol, Rosmarinus officinalis, Rubia cordifolia, Salvia miltiorrhiza, Saussaurea lappa, Schinus molle, Sida acuta, Silybum marianum, Simarouba glauca, Solanum melongena, Styrl-pyrone, Sutherlandia frutescens, Tabebuia impetiginosa, Tanacetum parthenium, Thymic peptides, Trifolium pratense, Ukrain, Vernodalin, Withania somnifera

Cancer Cell Lines		Therapeutic Agent
MCF-7aro	Invasive Ductal Carcinoma	Eugina jambolana
MDA-MB-231	Adenocarcinoma	Andrographis paniculata, Asimina triloba, Beauvericin, Beta-sitosterol, Boswellia, Camellia sinensis, Castanospermum australe, Centella asiatica, Cordyceps sinesis, Crocus sativus, Curcuma longa, Embelin, Emodin, Essiac, Eugenia jambolana, Evodia rutacarpa, Frondoside A, Ganoderma lucidum, Glyceollin, Gynura procumbens, I3C, Holothuroidea, Honokoil, Inonotus obliquus, Lactoferrin, Laetrile, Magnolia officinalis, Methyl jasmonate, Nigella sativa, Oridonin, Punica granatum, Rabdosia rubescens, Rheum palmatum, Rosmarinus officinalis, Salvia miltiorrhiza, Saussaurea lappa, Selenium Selenite, Stropanthus gratus, Tanacetum parthenium, Vernodalin, Vit K, Withania somnifera
MDA-MB-330	Carcinoma	Melatonin
MDA-MB-435	Adenocarcinoma	Casearia pulcherrima, Citrus pectin, Essiac, Frondoside A, Genistein, Honokoil, Magnolia officinalis, Simarouba versicolour ***see Notes**
MBA-MB-435S	Carcinoma	Accorus calamus, Carctol ***see Notes**
MDA-MB-436	Adenocarcinoma	Honokiol, Magnolia officinalis
MBA-MB-453	Carcinoma	Apigenin
MDA-MB-468	Adenocarcinoma	Contortrostatin, Glyceollin, Grifola frondosa, Melatonin, Quercetin, Rosmarinus officinalis, Sutherlandia frutescens, Trifolium pratense
SK-BR-3	Carcinoma	Arctium lappa, Frondoside A, Garcinia hanburyi, Rubia cordifolia, Magnolia officinalis, Silybum marianum, Ukrain
T47D	Transitional Epithelial Carcinoma	Artocarpus communis, Asimina triloba, Boswellia, DIM, Essiac, Magnolia officinalis, Melatonin, Salvia miltiorrhiza
ZR-75-1	Breast Ascites	Honokiol, Magnolia officinalis, Melatonin
***Notes-**	Gene expression studies have determined that the available MDA-MB-435 cells are of melanoma origin and not that of breast cancer. These pleural breast derived melanoma cells are from a M14 melanoma cell line and should not be used for research as a breast cancer cell line (see page 3)	
CENTRAL NERVOUS SYSTEM		
XF498	Neurocytoma	Rumex acetosella, Saussaurea lappa
CERVICAL		
Ca Ski	Epidermoid Carcinoma	Gynostemma pentaphyllum
HeLa	Epithelial Adenocarcinoma	Antrodia camphorata, Apigenin, Brazillian Red Bee Propolis, Broccoli sprout, Caesalpina pulcherrima, Combretum leprosum/Aspergillus oryzae, Commiphora myrrha, Coriolus versicolour, Cuminum cyminum, DIM, Fisetin, Frondoside A, Inonotus obliquus, I3C, Juglans nigra, Junipers communis/ Asperigilus fumigates, Luteolin, Nigella sativa, Physalis angulata, Plantago major, Saussaurea lappa, Selaginella tamariscina, Solanum melongena, Vanillin, Zeolite
KB	HPV Contaminated HeLa Cells	Halorosellinia/Guignardia
KBV200	Vincristine Resistant HPV HeLa Cells	Halorosellinia/Guignardia
SiHa	Carcinoma	Berberine, Cassia fistula, Mimusops elengi/Claviceps purpurea, Nigella sativa
CHOLANGIOCARCINOMA		
KKU-100	Ductal Carcinoma	Garcinia hanburyi, Mormordica charantia
KKU-M156	Adenocarcinoma	Garcinia hanburyi

BOTANICAL PLANT SOURCE & CYTOTOXIC CONSTITUENTS

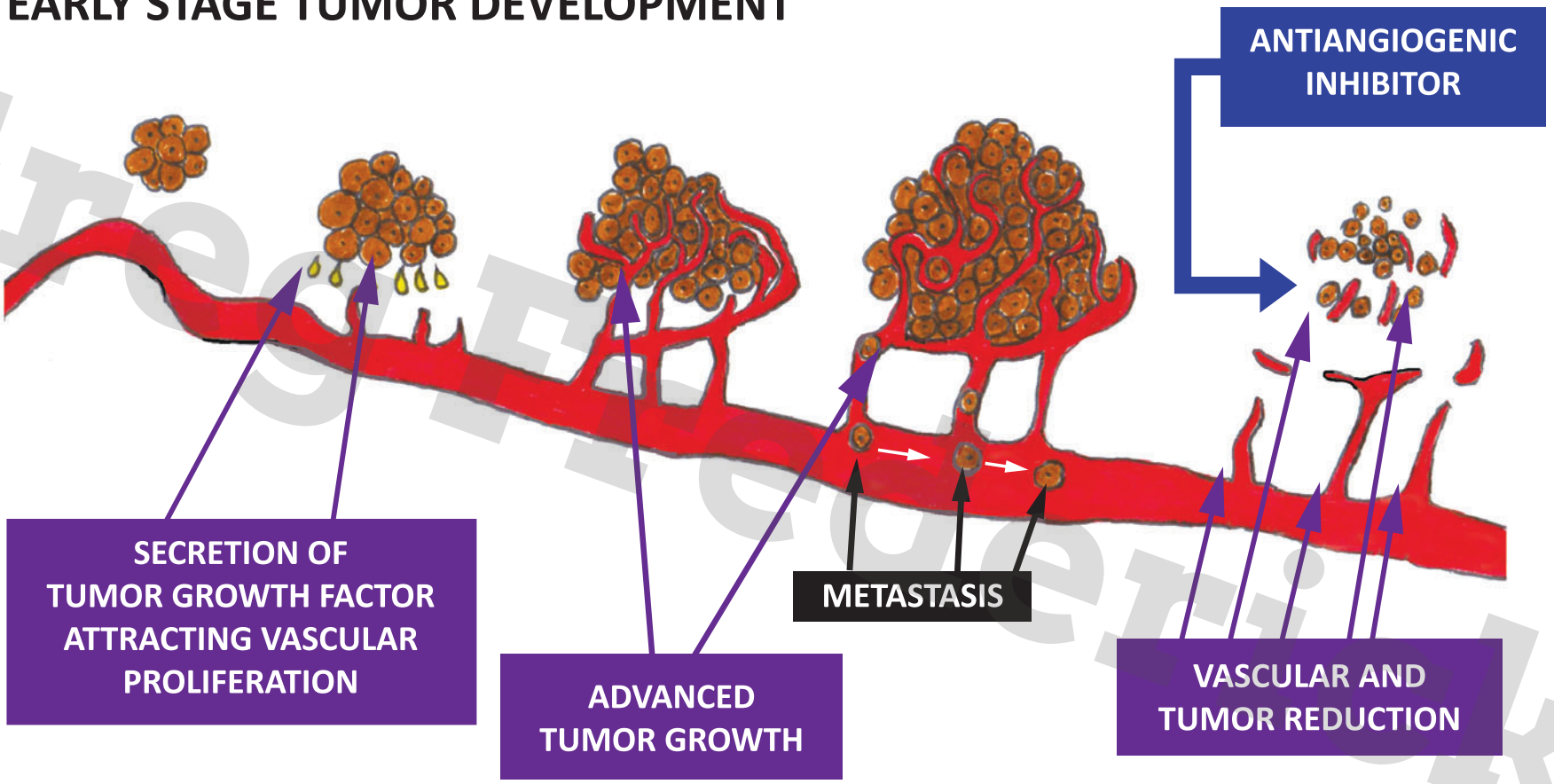
Therapeutic Plant Source	Cytotoxic Isolate
Acer nikoense	Corilagin, Geraniin, Ginnalin-A
Acorus calamus	Vincristine, Vinblastine
Agaricus blazei Murrill	α-glucans, β-glucans
Allium sativum	Ajoene, Allicin, Allium, Diallyl trisulfide, Germanium
Aloe-vera	Aloe-emodin
Andrographis paniculata	Andrographolide
Annona muricata	Annomuricin E, Annonaceous acetogenins, Isoquinoline
Antrodia camphorata	Antcin A, Antcin B, Antcin C, Benzoquinone, Methylantcinate A,
Arctium lappa	Arctiin, Arctigenin, Lappaol F, Matairesinol, Secoisolariciresinol
Argimonia species	Apigenin, Epigallocatechin-3-gallate(EGCG), Isocoumarin, Isorhamnetin, Kaempferol, Luteolin, Quercetin
Artemisia annua	Artemisinin
Artocarpus species	Artocarpin, Isolesperol
Asimina triloba	Acetogenins, Benzyl isothiocyanate
Asparagus officinalis	Asparanin A
Astragalus membranaceus	Formononetin
Bidens pilosa	Heptatriene, Luteolin, Vanillin
Boswellia species	Acetyl-11-keto-beta-boswellic acid (AKBA), Boswellic acid, Diterpene, Sesquiterpene
Brazilian Red Bee Propolis	Napthoquinone, Pterocarpan, Triterpenoids
Broccoli Sprout Extract	Glucoraphanin, Sulforaphane
Bulnesia sarmientoi	(-)-Epicatechin
Caesalpinia bonducella	Bonducin, Caesaldekarin, Caesalpin, Diosgenin, Methylcaesalpinaone, Myristic acid
Caesalpinia pulcherrima	Pulcherrimin B, Pulcherrimin C
Camellia sinensis	Epigallocatechin-3-gallate(EGCG), Epicatechin-3-gallate(ECG)
Cannabis indica	Anandamide, Cannabidol, Cannabidiol, Cannabidiolic acid, Cannabidvarin
Carnivora	Plumbagin
Casearia species	Argutin B, Casearins A-S, Lapachol
Cassia fistula	Anthraquinone, β-sitosterol, Fistulin, Kaempferol, Lupenol, Rhein
Castanospermum australe	Castanospermine
Catharanthus roseus	Vincristine, Vinblastine, Vindesine,Vinorelbine
Cayaponia tayuya	Cayaponoside, Curcurbitacin B, Dihydrocurcurcitacin B
Centella asiatica	Asiatic acid, Asiaticoside

Illustration 3



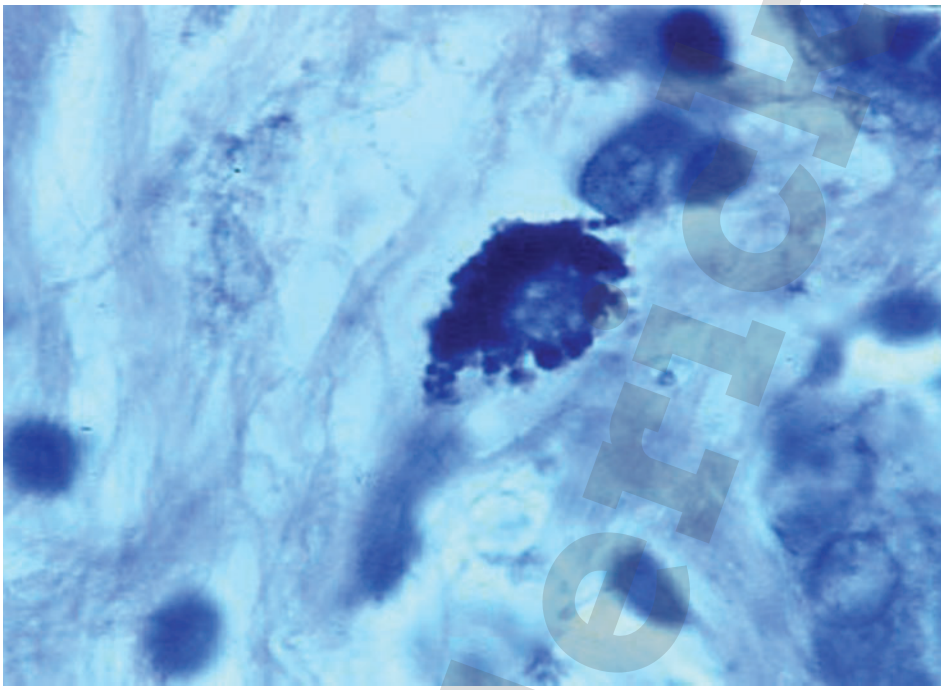
Electron scanning micrograph of the so-called "plasmalytic forms" or chondrit as they emerge from the erythrocyte. It is very evident in this picture that the chondrits penetrate the membrane and are not just on or in the erythrocyte. This process is quickened when the sample is heated or aged. These are observed in darkfield as either white or yellow strands. These are observed accompanying tumors and/or dental foci.

REFERENCE:
From Baker, R.F., J. Ultrastruct. Res., 11,494-507, 1964



ANGIOGENESIS AND ANTIANGIOGENESIS

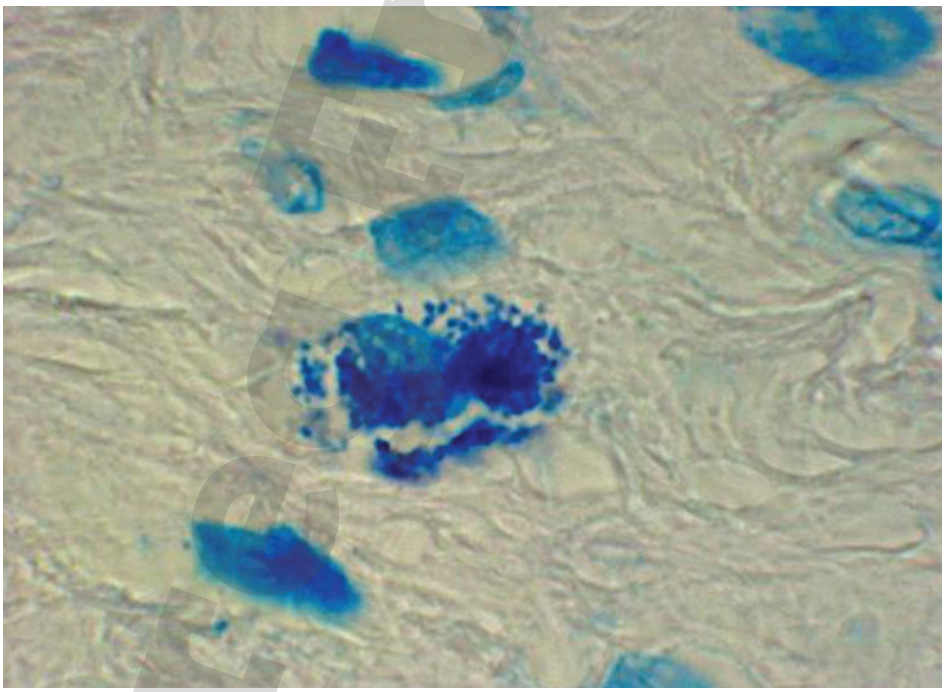
Illustration 6



Intracellular variably-sized coccoid forms in breast cancer from the work of Virginia Livingston Wheeler

Courtesy of Alan Cantwell MD

Illustration 7



Intracellular bacteria in prostate cancer from the work of Virginia Livingston Wheeler

Courtesy of Alan Cantwell MD

NOTABLE PEOPLE IN CANCER RESEARCH

J. Weldon Fell (1808-1887)

- Original member of the New York Academy of Medicine.
- Believed cancer is a constitutional disease.
- He wrote “Treatise of Cancer” (1857).
- Learned Indigenous cancer cures from a Native American.
- First white physician to use black salve incorporating bloodroot, zinc chloride, flour and water.
- Developed tumor therapy using incisions and salve.
- Forced to leave America and set up cancer practice in England.

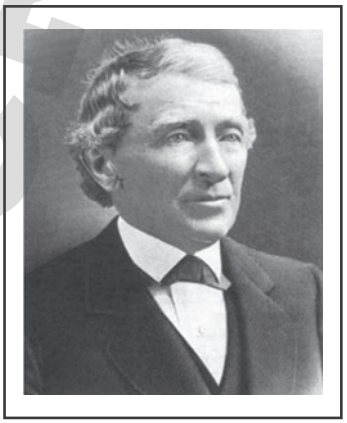


Photo credit: http://mchistory.org/research/resources/jesse-w-fell.php

Claude Bernard (1813-1878)

- French Physiologist and father of modern pathology.
- Introduced concept of terrain and originated the term “Mileu intérieur” and believed disease started within the body.
- First to use blind experiments to ensure objectivity of test results.
- He disapproved of biologists who manipulated their data to promote false cures.
- Originator of quantitative lab testing and the concept of homeostasis.
- Proved Pasteur’s germ theory inadequate.

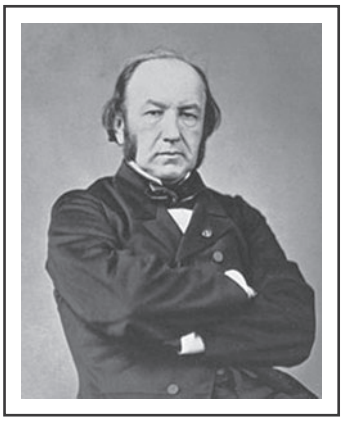


Photo credit: https://en.wikipedia.org/wiki/Claude_Bernard

Antoine Bechamp (1816-1908)

- Father of New Biology and bitter rival of Louis Pasteur.
- Promoted the concept of terrain and discovered microzymas.
- Believed that disease started from toxins and an unhealthy terrain.
- Plagiarized by Louis Pasteur.
- More achievements and awards than any biologist/ scientist in history.
- Synthesized the first arsenical drug which later became the first chemotherapy under Paul Ehrlich.
- Omitted by all orthodox medical & encyclopedic reference material.

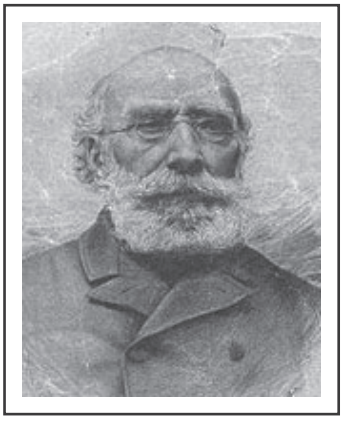


Photo credit: https://en.wikipedia.org/wiki/Antoine_B%C3%A9champ

William Russell (1852-1940)

- Scottish Pathologist and Physician.
- First to describe “a characteristic organism of cancer” or “fushisine bodies“ because of their bluish-red staining qualities.
- He found a fungal or yeast-like parasite he originally called “blastomycete” in cancer tumors.
- Remembered today in orthodox medicine by “Russell bodies” believed to be immunoglobulins rather than bacterial or fugal forms found in cancer tumors.

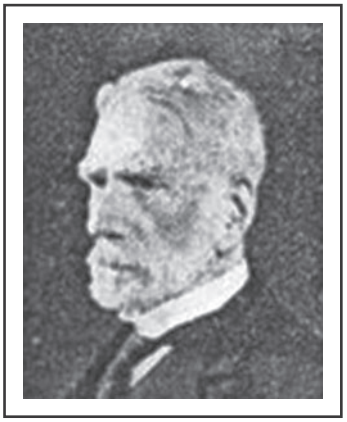


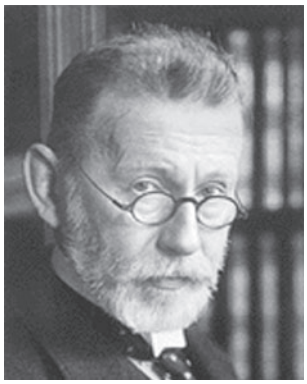
Photo credit: http://www.odermatol.com/issue-in-html/2013-3-33-eponyms/

Louis Pasteur (1822-1895)

- French Chemist and Microbiologist
- Father of Pharmaceutical Medicine.
- Renowned for his principles of vaccination.
- Plagiarized research of Bechamp concerning microbial fermentation and then attempted to discredit him.
- Promoter of "Germ Theory" that disease comes from outside invaders and that drugs, vaccines and surgery were the only cures.
- Believed bacteria could not change (Monomorphism).
- Developed pasteurization which kills bacteria and enzymes needed for digestion.

Photo credit: https://www.britannica.com/biography/Louis-Pasteur

Paul Ehrlich (1854-1915)



- German Physician/Scientist/Haematologist/ Immunologist
- Developed and named the concept of chemotherapy and cancer vaccination by injecting weaker cancer cells to generate immunity to cancer.
- Invented gram staining to microscopically identify different blood cells.
- Discovered ascites and reported that if the primary tumor is removed, then metastasis precipitously increases.
- Received Noble Prize in medicine in Immunology.

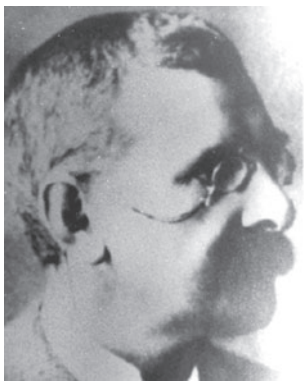
Photo credit: http://www.ehrlich2004.org/aboutpaulehrlich_e.htm

Emil von Behring (1854-1917)

- German Physiologist.
- Developed concept of vaccines.
- Discovered diphtheria antitoxin in 1890. Developed colloidal silver to treat disease.
- Developed serum therapy-by injecting disease into the animal then injecting the blood of that animal into another precursor to induce immunoglobulin E therapy against cancer (immunotherapy).
- Received Noble Prize in Physiology

Photo credit: https://www.iitvidya.com/emil-von-behring/

John Beard (1858-1924)



- Scottish Embryologist.
- Found pancreatic enzymes regulate placental development similar to the growth of cancer tumors.
- In 1911 published "The Enzyme Therapy of Cancer".
- He created injectable pancreatic enzymes for tumor regression.
- After Beards' death in 1924 Enzyme Therapy was forgotten for decades.
- Nominated for Nobel Prize in Medicine in 1906 for research on enzyme therapy.
- *Photo credit: www.Infograph.venngage.com*

ABOUT THE AUTHOR

Greg Fredericks B.A. M.A. N.D. N.M.D.

Greg Fredericks received his Bachelor Degree with honors from the University of New Brunswick in 1976 after enrolling in Pre-Medical Studies. In 1982 he received a Masters Degree in Psychology from the University of St Louis, Missouri. After a long illness his direction changed to Natural Medicine and he pursued a Doctorate in Naturopathy from the British College of Naturopathy in 1986. Greg became an educator/formulator for Biotec Corp and Aveda Aromatherapy in Calgary, Canada from 1987-1993 and later received a Diploma in Nutrition and Natural Health in 1995 from Bastyr College and subsequent Diplomas in TCM from the Chinese Herbal Institute in San Jose, CA (1997) and in Pathology from the Western Australian School of Pathology in 1999.

Greg was fortunate to train with some outstanding practitioners in the 1980's and 90's including Gaston Naessens, Bernard Jensen, Dr. med. Maria M. Bleker and others. He has multiple certifications in Iridology and Blood Analysis from various disciplines around the world. He has lectured internationally on behalf of Sanum-Kehlbeck GmbH & Co. Germany from 1997-2001. Greg has been the Director of Nu-Look Biologics since 1997. His articles have appeared in Explore for the Professional (USA), Nexus and Sanum (AUS).

His Natural Medicine Radio Show in Perth WA (1999) lasted one year and was terminated mid broadcast while announcing that Statin drugs were potentially carcinogenic.

He moved to the East Coast of Australia in 2002 where he set up clinic in Lennox Head NSW where he continues to practice.

Greg has always maintained the philosophy that successful healing and wellness is only obtained by considering the individual traits of each unique person. One size fits all approaches fall short in delivering the assistance needed for individuals to regain healthy balance in their life. Greg has developed a range of diagnostics that are all performed in his microscopy lab and results are given in a form of a take home "owners guide". This individual guide includes physical/constitutional information dependant on personality and lifestyle traits, blood type and other factors that will support the individual to attain optimum wellness.

In his over 30 years of practice, Greg has done over 70,000 consultations. He has lectured at NEXUS 2014 and the Australian Association of Colon Hydrotherapists. Greg is the author of the 3rd Edition of Darkfield Warriors: The Definitive Guide to the World of Darkfield Live Blood Microscopy and is considered an international authority on the subject. He is a member of the American Naturopathic Medical Association, and was recently appointed State Representative of NSW, Australia for the Complementary Medicine Association (CMA) for 2017- 2019.

Greg is the father of four beautiful children; Enya, Taine, Rafe and Saffron and currently resides in the Northern Rivers region of New South Wales.

The author has presented the material in this book without predjudice and without influence from special interest groups or corporate renumeration.