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We all crave adventures big and small that make our life complete: the venture of starting a family, obtaining a degree, beginning a career, forming a relationship, building a business, or developing an artistic talent. These can all be exciting rides with ups and downs and frighteningly scary moments, just like a carnival ride. At the end of each of these adventures, there is that reward and heightened feeling of being alive or having done something worthwhile. During the last 15 years, As an Advanced Integrative Medicine Authority I had the opportunity to work with many wonderful Integrative researchers and doctors. For each of them, their cutting-edge research or practice was their adventure. Some gave up a safe job to take on the risk of a new revolutionary research, science or practice to meet the demand and cater to an aging population and a high number of patients suffering from chronic diseases. Getting on that carnival ride was the manifestation of a dream or the search for validation that spurred them on; it was rarely about money or simple business transactions. Revealing, analyzing, inspiring people, treating people with chronic ailments, selling making the Earth and themselves healthier, harnessing the sun and wind. Many of these ventures have survived, grown and evolved into something great. Some simply served their purpose and vanished.

Adventures begin and end, for the past 4 decades I dedicated my life to finding innovations through healing adventures for myself and for thousands of sick individuals who relied on the revolutionary treatments that I provided. Finally, this particular ride landed on Cutting-edge Medical scientific discoveries that Create a Huge Impact on Worldwide Healthcare. One of the most remarkable breakthroughs is the take-off of human exosomes and peptides to regenerative medicine. Exosomes are derived from placental and adipose derived stem cells, then are flawlessly used to

a wide array of diagnostic and medicinal applications enabling better diagnosis and faster healing, stem cell differentiation and tissue regeneration.

I truly believe that health is wealth. No matter what trials and tribulations we face each day, if we don't have our health, nothing else matters. Thanks to the integrative medical professionals in our community, we have amazing resources for our well-being. As a health professional, you want to know the latest in medical science, but you also want to understand how your business can become more successful and more productive. We understand how precious your time is, we crafted The HealPreneur Platform and articles will cover Spirit, Mind and Body: how the healer can be healed. We will offer advice on how to market, sell or fund your business. We will look at a style for you and your center, we will show you how to give your patients a good experience from the second they walk in your door. We will provide access to the resources you need, from coaches and trainers to technology to artists who can supply the artwork for your center all in one place so they can grow themselves and their business.

We're excited to feature Dr. Robert Goldman, the cocreator of the 280 Billion USD\$ Anti-Aging Industry in this special issue.

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Enjoy this edition of HealPreneur. If you have an article, please contact us at DrDalalAkoury@healpreneur. com, we welcome your contributions. If you would like to see something featured drop us a line, we would love to hear your ideas. Read about the latest health trends. Visit www.Healpreneur.com for digital copy.

Wishing you good health, good times and the best, always.

Don't forget to wear green on March 17, and enjoy the Miracles of Exosomes and proteins

Breast Cancer Treatment Strategies: A Short Overview Jesse A. Stoff, MD

Health may be defined as a congruent alignment of ones' physical, emotional, mental, social, spiritual and environmental milieu. For a cancer to occur there has to be a serious, prolonged disruption in one or more aspects of the individuals' circumstances. Genetics may predispose one to a specific type of cancer but by only a relatively small percentage of increased risk.

For the cancer to develop it needs a trigger, and a series of promoters, against which the body has a number of redundant protective mechanisms. Ultimately, for any cancer to develop, or recur, there has to be a significant failure of one or more pathways within the immune system. This is why Immunotherapy and the field of Onco-Immunology are so prominent in the war against cancer. But, the immune system doesn't exist and operate in a vacuum. For it to be fully functional it needs, amongst other things, an intact biochemistry. By assessing an individual's immune structure and function as well as their hormone balance and biochemical markers a personalized treatment strategy becomes evident which, when specifically applied, gives the best possible outcome for the quality and quantity of life. Different treatment strategies may be used based upon the individual's blood

test results and the genetics of the cancer. The common thread of these strategies is that they are all ultimately designed to stop and reverse the cancer. These strategies, in general, may be used against any type of cancer but this short article will focus more on breast cancer.

From a perspective of 10,000 feet there are two basic characteristics of breast cancer; genetic instability and the propensity to metastasize. From those two basic observational characteristics, The Hallmarks of Cancer were derived by Dr's Hanahan and Weinberg in 2000 as:

- o Self-sufficiency in growth signals
- o Insensitivity to anti-growth signals
- o Evading apoptosis
- o Limitless replicative potential
- o Sustained angiogenesis
- o Tissue invasion and metastasis.

And then added to in 2011:

- o Deregulating cellular energetics
- o Avoiding immune destruction
- o Genome instability and mutation
- o Tumor-promoting Inflammation (1,2).

As a starting point to help my patients who are fighting breast cancer, there are a few supplements one can use until lab tests and

cancer genetic studies are completed. Once the tests and studies are finalized and returned, a more specific treatment strategy can be formulated to address the above hallmarks. Each of these supplements has a multitude of beneficial effects but, chief among them is their ability to stabilize genetics, creating the foundation of an integrative anti-cancer strategy. During the course of oncogenesis and tumor progression, breast cancer cells constitutively up-regulate signaling pathways relevant to cell proliferation as a result of any number of genetic mutations. It's that genetic instability that leads to breast cancer being cancer in the first place and it's those mutations which account for the multiple cell lines that compose every tumor. Stabilizing the cancer's genetics is thus an important first step.

First on our list of genetic stabilizers is Vitamin D. In addition to enhancing DNA repair, Vitamin D also induces growth arrest and cell death (apoptosis) of tumor cells. Cell-based studies show that the active metabolite 1,25 dihydroxyvitamin D is the biologically active form that works through the vitamin D receptor to regulate gene activity. Vitamin D (D3) is produced from 7-dehydrocholesterol when skin is directly exposed to UVB light which, in more northern locations is largely filtered out by the atmosphere. Vitamin D is readily sourced from various foods including; fish, eggs, caviar (for the gourmets amongst us), some mushrooms, beef liver, and cheese. Regardless of whether vitamin D comes from the skin or the diet, vitamin D3 is transported through the blood by the Vitamin D Binding Protein (DBP). Once delivered to the liver, vitamin D is hydroxylated on its side chain to form 25 hydroxyvitamin D (25OH D). This is a stable metabolite whose serum levels are commonly used to assess vitamin D status. As needed and if available, D3 circulates to the kidneys which is the primary site where the active form of vitamin D, 1,25(OH)2 D, is produced. Through its effect on genes it inhibits cell cycle progression and tumor cell growth. Mechanisms of action range from preventing cell proliferation (cell cycle arrest) in cancer cells to inducing cell death (apoptosis) or suppressing cell adhesion molecules and growth factors that promote cellular homing and metastasis. It also affords important antioxidant protection and serves as an immunomodulator of the immune system (3-7).

Next comes Indole-3-carbinol and its metabolite 3,3'-diindoylmethane (DIM) which are critically important, on several levels, when fighting breast cancer. They target multiple aspects of the cancer cell cycle to stabilize it and its response to hormones. When methylation detox pathways start to fail in the body, certain regions of the genes will accumulate too many methyl groups which can lead to increased mutations and eventual cancer development. Much research has demonstrated how DIM reduced methylation and the risk of mutations occurring. For example, in split population studies, mice given TRAMP cancer cells were also given DIM. The mice given the DIM showed a much lower incidence of breast cancer and metastasis than controls (8-14).

Curcumin, a component of turmeric (Curcuma longa), is a low molecular weight molecule that has antiproliferative activity and inhibits tumor initiation and propagation through a variety of pathways. It accomplishes this through several biochemical (epigenetic) effects that result in genetic modulation that then changes the expression of several key proteins that can result in the death of cancer cells.

p53 (TP53) is a tumor suppressor gene that is responsible for protecting cells from tumorigenic alterations. Mutational inactivation of p53 is frequently observed in many cancers and is the most common mutation in breast cancer. Curcumin selectively increases p53 activity in cancer cells which then results in cancer cell death.

Curcumin also induces the up-regulation of carcinogen-detoxifying enzymes which have anti-oxidation effects, and reduce the level of inflammation and the stimulation of cancer stem cells. Real time animal model studies have demonstrated that curcumin also decreased the activity of DNA damaging genes which is but part of the reason for curcumin's induced growth inhibition of cancer cells (14-16).

Sulforaphane (SFN) is a substance found in cruciferous vegetables such as broccoli,

Brussels sprouts, cauliflower, and cabbage. Experimentally, in cell cultures and animal models, SFN was shown to be a highly effective chemoprotective against, carcinogen-induced and genetic animal cancer models, as well as in transplant models of cancer. The early research focused on the detoxification ability of SFN to induce liver detoxifying enzymes. Later studies showed that SFN could cause apoptotic cancer cell death. Furthermore, it leads to the activation of special genes including tumor suppressor genes. The effect on cancer genetics is profound and therapeutically beneficial (17-21).

Fish oil rounds out our list of top genetic stabilizing supplements. One of many changes that occur to the breast cancer cell's biochemistry and genetics is in the production, metabolism and expression of MicroRNAs (miRNAs). First discovered in the early 1990's their importance as a distinct class of biological regulators wasn't appreciated for another decade. MicroRNAs (miRNAs) are short molecules just 21-25 nucleotides long but can have powerful effects on gene expression. More than 2000 miRNAs have been identified including many specific miRNAs that have been found to be associated with diseases states including cancer and the risk of metastasis. The identification of circulating miRNA specific to metastatic cancer presents a unique opportunity for early disease identification and for monitoring disease burden as a circulating biomarker. Furthermore, there is a growing body of evidences on the value of miRNAs associated with the development of drug-resistance, suggesting their values, once targeted, as a potential approach to overcoming chemo-resistance. Fish oil can modulate the expression of the miRNAs including significantly reducing the risk of metastasis. Additionally, fish oil, like the other supplements described have many other anti-cancer effects, miRNA's that are absorbed into our blood stream from GMO foods are currently being studied for their oncogenic potential as they are normally foreign to human biology (22-27).

Once the basic genetic stabilizers are in place we move on to more specific, integrative, breast cancer treatment strategies which are based upon laboratory results, the patient's history and our clinical experience. Integrative anticancer strategies are based upon the basic observation that for a patient to develop a serious cancer multiple systemic abnormality must be occurring simultaneously; genetically, biochemically, immunologically and hormonally which must be addressed from a functional medicine point of view. An effective treatment strategy addresses these issues while applying pressure against the weak points of the cancer, as determined through laboratory and genetic testing, to buy the time necessary to reconstitute an effective immune response that leads to a durable remission. Assuming that the physician has a good understanding of immunology and biochemistry and a thorough, if not specialized, knowledge of oncology then these strategies can be added to their armamentarium in a matter of days or weeks of workshops, conferences and additional study. There are a number of anticancer strategies that can be employed, which to use when is a matter of objective data collection balanced by experience. Again, in no particular order, as anyone of them could be potentially be the one key strategy needed for a particular patient to go into remission but, generally. multiple strategies are needed and are timed to the changing conditions clinically as treatment progresses.

References:

- 1) Hanahan D, Weinberg RA. Hallmarks of cancer: the next generation. Cell 2011;144:646-74.
- 2) Hanahan D, Weinberg RA. The hallmarks of cancer. Cell 2000;100:57-70.
- 3) Fleet JC, DeSmet M, Johnson R, et al. Vitamin D and cancer: a review of molecular mechanisms. Biochem J 2012;441:61-76.
- 4) Pandolfi F, Franza L, Mandolini C, et al. Immune modulation by vitamin D: special emphasis on its role in prevention and treatment of cancer. Clin Ther 2017;39:884-893.
- 5) Chatterjee M. Vitamin D and genomic stability. Mutat Res 2001;475:69-87.
- 6) Vuolo L, Di Somma C, Faggiano A, et al. Vitamin D and cancer. Front Endocrinol (Lausanne) 2012;3:58.
- 7) Bikle DD. Vitamin D and cancer: the promise not yet fulfilled. Endocrine 2014;46:29-38.
- 8) Thomson CA, Ho E, Strom MB. Chemopreventive properties of 3,3'-diindolylmethne in breast cancer: evidence from experimental and human studies. Nutr Rev 2016;74:432-443.
- 9) Safe S, Papineni S, Chintharlapalli S. Cancer

chemotheraphy with indole-3-carbinol, bis(3'-indolyl) methane and synthetic analogs. Cancer Lett 2008;269:326-338.

- 10) Weng JR, Tsai CH, Kulp SK, et al. Intole-3-carbinol as a chemopreventive and anti-cancer agent. Cancer Lett 2008;262:153-163.
- 11) Rahman KM, Ali S, Aboukameel A, et al. Inactivation of NF-kappaB by 3,3'-diindolylmethane contributes to increased apoptosis induced by chemotherapeutic agent in breast cancer cells. Mol Cancer Ther 2007;6:2757-2765.
- 12) Palomera-Sanchez Z, Watson GW, Wong CP, et al. The phytochemical 3,3'-diindolylmethane decreases expression of AR-controlled DNA damage repair genes through prepressive chromatin modifications and is associated with DNA damage in prostate cancer cells. J Nutr Biochem 2017;47:113-119.
- 13) Watson GW, Beaver LM, Williams DE, et al. Phytochemicals from cruciferous vegetables, epigenetics, and prostate cancer prevention. AAPS J 2013;15:951-961.
- 14) Ravindran J, Prasad S, Aggarwal BB. Curcumin and cancer cells: how many ways can curry kill tumor cells selectively? AAPS J 2009;11:495-510.
- 15) Park W, Amin AR, Chen ZG, et al. New perspectives of curcumin in cancer prevention. Cancer Prev Res (Phila) 2013; 6:387-400.
- 16) Ji Z. Targeting DNA damage and repair by curcumin. Breast Cancer (Auckl) 2010;4:1-3.
- 17) Tortorella SM, Royce SG, Licciardi PV, et al. Dietary sulforaphane in cancer chemoprevention: the role of epigenetic regulation and HDAC inhibition. Antioxid Redox Signal 2015;22:1385-1424.
- 18) Clarke JD, Hsu A, Yu Z, et al. Differential effects of sulforaphane on histone deacetylases, cell cycle arrest and apoptosis in normal prostate cells versus hyperplastic and cancerous prostate cells. Mol Nutr Food Res 2011;55:999-1009.

- 19) Clarke JD, Dashwood RH, Ho E. Multi-targeted prevention of cancer by sulforaphane. Cancer Lett 2008;269:291-304.
- 20) Cho SD, Li G, Hu H, et al. Involvement of c-Jun N-terminal kinase in G2/M arrest and caspase-mediated apoptosis induced by sulforaphane in DU145 prostate cancer cells. Nutr Cancer 2005;52:213-224.
- 21) Baier SR, Zbasnik R, Schlegel V, et al. Off-target effects of sulforaphane include the derepression of long terminal repeats through histone acetylation events. J Nutr Biochem 2014;25:665-668.
- 22) Berguin IM, Edwards IJ, Chen YQ. Multi-targeted therapy of cancer by omega-3 fatty acids. Cancer Lett 2008;269:363-377.
- 23) Jiang Y, Djuric Z, Sen A, et al. Biomarkers for personalizing omega-3 fatty acid dosing. Cancer Prev Res (Phila) 2014;7:1011-1022.
- 24) Fabian CJ, Kimler BD, Phillips TA, et al. Modulation of breast cancer risk biomarkers by high-dose omega-3 fatty acids: phase II pilot study in postmenopausal women. Cancer Prev Res (Phila) 2015;8:922-931.
- 25) Khadge S, Thiele GM, Sharp JG, et al. Long-chain omega-3 polyunsaturated fatty acids modulate mammary gland composition and inflammation. J Mammary Gland Biol Neoplasia 2018;26:43-58.
- 26) McGuire A, Brown JA, Kerin MJ. Metastatic breast cancer: the potential of miRNA for diagnosis and treatment monitoring. Cancer Metastasis Rev 2015;34:145-155.
- 27) Hardman WE. Omega-3 fatty acids to augment cancer therapy. J Nutr 2002;132:3508S-3512S.

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Dr. Jesse Stoff is an internationally renowned physician, with extensive credentials in clinical immunology, and holistic medicine. A graduate of New York Medical College, he pursued extensive post-doctoral training including a fellowship at the Royal London Homeopathic Hospital in London, England. He has authored/co-authored dozens of articles and 9 books including co-authoring the bestsellers Chronic Fatigue Syndrome: The Hidden Epidemic and The Prostate Miracle. He has also served as a member of the Clinical Nutrition Board of Cancer Treatment Centers of America, Inc. and he taught CME courses in Clinical Immunology at the University of Arizona. He is frequently invited to give specialized lectures at national and international medical conventions. As Medical Director of the Stoff Institute for Medical Research, he consults with physicians and medical groups both domestically and abroad on the subjects of immune system disorders and immune reconstitution. As a result of his research, in the field of immunology, he has developed several new molecular complexes, one of which is now being patented as a true anti-biotic replacement.