Reducing Risk, Recurrence, and Treating the Underlying Cause of Breast Cancer

Ronald L. Stram, MD
Stram Center for Integrative Medicine

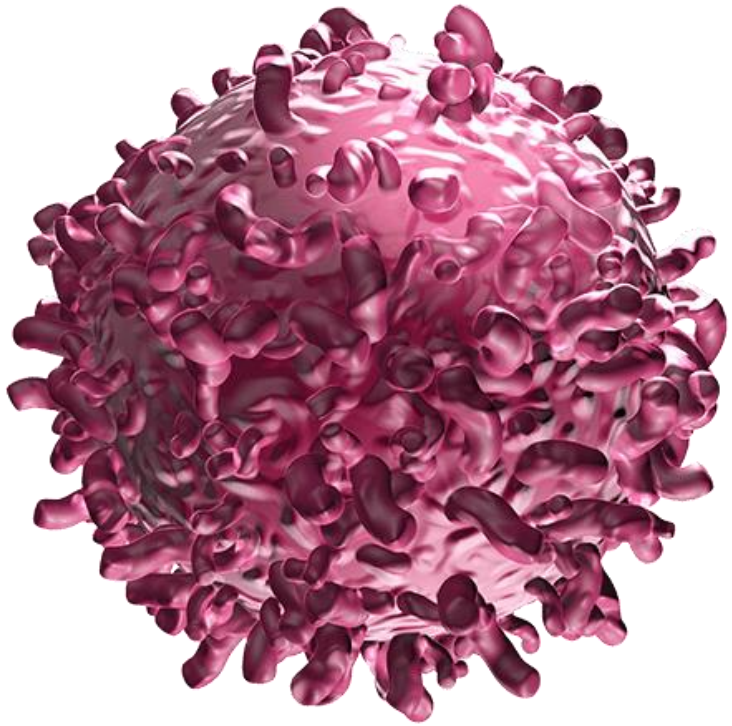
Cancer development and progression is a complex process that involves a host of functional and genetic abnormalities

- ***Epigenetic modification:*** DNA methylation, histone acetylation, genomic mutations and altered gene expression resulting in a change in overall cell function.

- ***Cancer cells***: contain full complement of bio-markers necessary for survival: proliferation, differentiation, cell death and expression of cell type function.

- ***Cancer cells:*** Lack the enzyme, catalase, needed to convert H202 to 02 and H20

- ***Cancer cell:*** altered regulation of cell function



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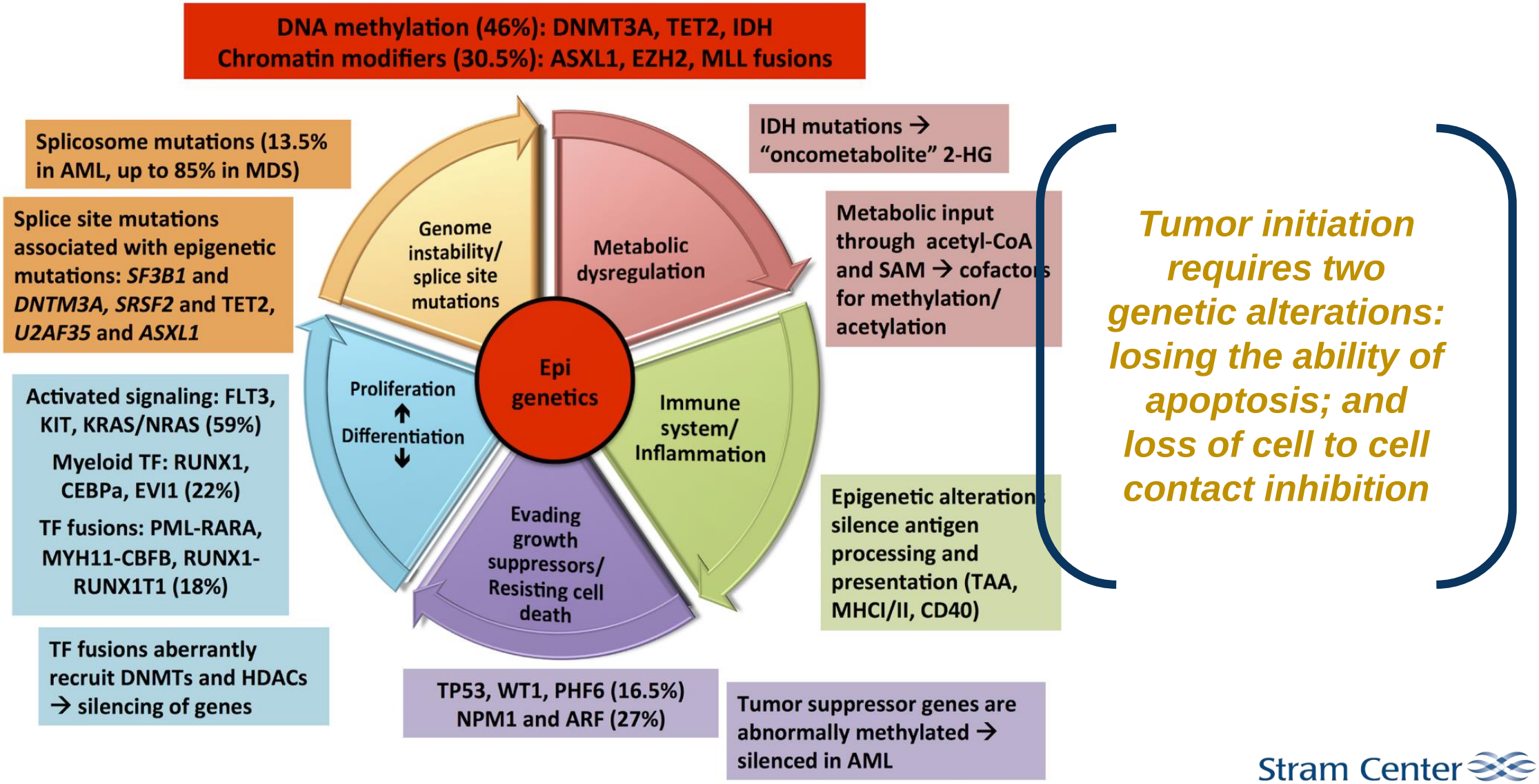
Tumor Initiation and Growth Disinhibition



Tumor initiation requires two genetic alterations: losing the ability of apoptosis; and loss of cell to cell contact inhibition

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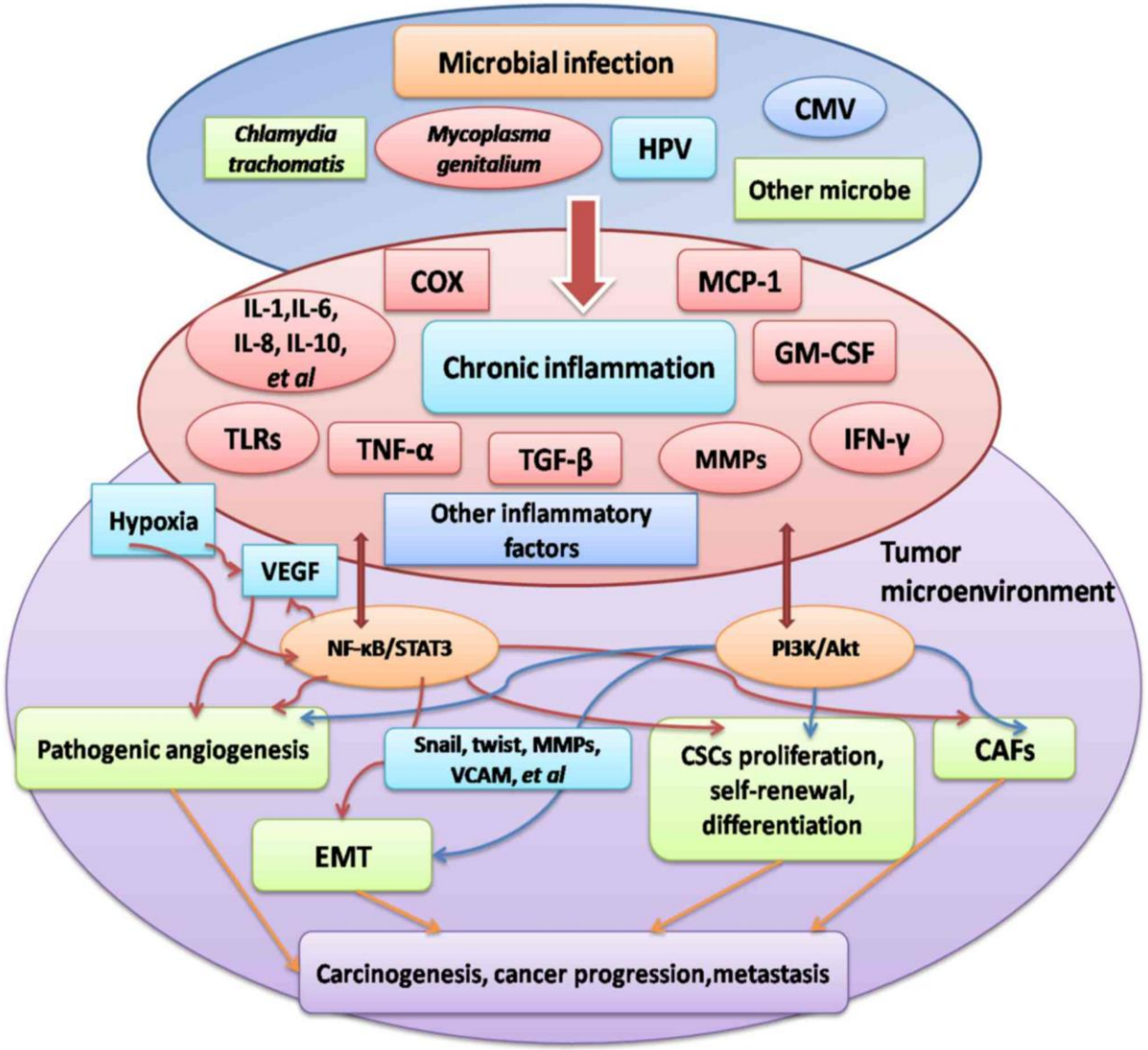
Host Immune Response to Infection and Cancer: Unexpected Commonalities

Inflammation and Cancer



25 % of all cancers have a known infection or infection associated chronic inflammation

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Bartonella is able to produce tumours

Current Knowledge of *Bartonella* Species

M. Maurin, R. Birtles, D. Raoult*

Bartonella species are now considered emerging pathogens. Of the 11 currently recognized species, four have been implicated in human disease, although only two have been encountered in Europe. *Bartonella quintana* infections are now being diagnosed among the urban homeless and deprived, manifesting as trench fever, and *Bartonella henselae* has been shown to be the causative agent of cat scratch disease. Both species also cause a variety of HIV-associated infections, including bacillary angiomatosis. However, perhaps the most significant presentation of bartonellae infection is culture-negative endocarditis. The epidemiologies of *Bartonella* infections are poorly understood; most *Bartonella henselae* infections are probably acquired from infected cats, either directly by contact with a cat or indirectly via fleas. No animal reservoir has been implicated for *Bartonella quintana*; however, infection can be transmitted via the human body louse. Diagnosis of *Bartonella* infections can be made using histological or microbiological methods. The demonstration of specific antibodies may be useful in some instances, although certainly not in all. Cultivation of *Bartonella* is difficult, as the bacteria are extremely fastidious. Polymerase chain reaction-based or immunological methods for the detection of bartonellae in infected tissues have proven useful. Clinical relapse is often associated with *Bartonella* infections despite a wide range of prescribed regimens. Only aminoglycosides display in vitro bactericidal activity against intracellular *Bartonella* species; therefore, they are recommended for treatment of *Bartonella* infections.

Human infections due to *Bartonella* species are widely considered emerging diseases. They include long-recognized diseases such as Carrion's disease (classic bartonellosis), trench fever, and cat-scratch disease and newer clinical manifestations such as bacillary angiomatosis, peliosis hepatitis, septicemia, endocarditis, chronic lymphadenopathy, and neurologic disorders. New molecular biology techniques, mainly based on 16S rRNA gene amplification and analysis, have allowed recognition of the role of *Bartonella* (formerly *Rochalimaea* species in a number of these isms. The most striking pathological feature of *Bartonella* infection is the apparent ability of these bacteria to produce angioproliferative lesions in immunocompromised patients, such as those infected with HIV. Capillary and endothelial cell proliferations are characteristic histologic findings of bacillary angiomatosis, peliosis hepatitis, and classic bartonellosis. Bartonellae are the only known bacteria with the ability to produce angiogenic tumors in humans, although *Agrobacterium* species, which belong to the same phylogenic group as *Bartonella* species, produce tumors in plants.

"Bartonellae are the only known bacteria with the ability to produce angiogenic tumors in humans"

Source:_ Maurin, Max & Birtles, Richard & Raoult, D. (1997). Current knowledge of Bartonella species. European journal of clinical microbiology & infectious diseases

What are Microbes?

***Microbes*: organisms that are too small to be seen with the naked eye**

2-3 TRILLION

The human microbiome is made up of more than 2-3 trillion bacteria, fungi, protozoa, and viruses that live in and inside the body

1-2X

We have 1-2 times more microbial cells in our body than human cells and the majority live in our guts- especially the large intestine, or colon

The bacteria in our microbiomes are essential to human health and aid in biological processes such as:

- $E=mc^2$ — Extracting energy from food
- RETINOL, FOLATE, RIBOFLAVIN, BIOTIN, NIACIN — Producing essential vitamins
- Regulating our immune system
- Regulating our glucose levels and metabolism
- Protecting us against disease-causing microbes

SYMBIOTIC

The beneficial and symbiotic relationship between humans and our microbiomes has likely evolved and changed throughout human development.

Personal microbial communities shift throughout a person's life and are influenced by diet, exercise, medications such as antibiotics, pathogens, and other environmental factors.

Microbiome

Endo-Biome:

Microbiome	controls production, inhibits or supports hormonal balance.
Depression	initiates production of serotonin, dopamine and norepineprine
Polycystic ovary/ endometriosis/ Menses / Menopause/ breast cancer/ prostate cancer	produces all three estrogens : estrone, estradiol and estriol (estriol- protective against osteoporosis and menopause symptoms) and progesterone.
Correcting dysbiosis	may be the key for preventing or reversing estrogen related conditions

History of FMT

Ancient China

Oral use of human fecal material for food poisoning or severe diarrhea

Veterinary Medicine

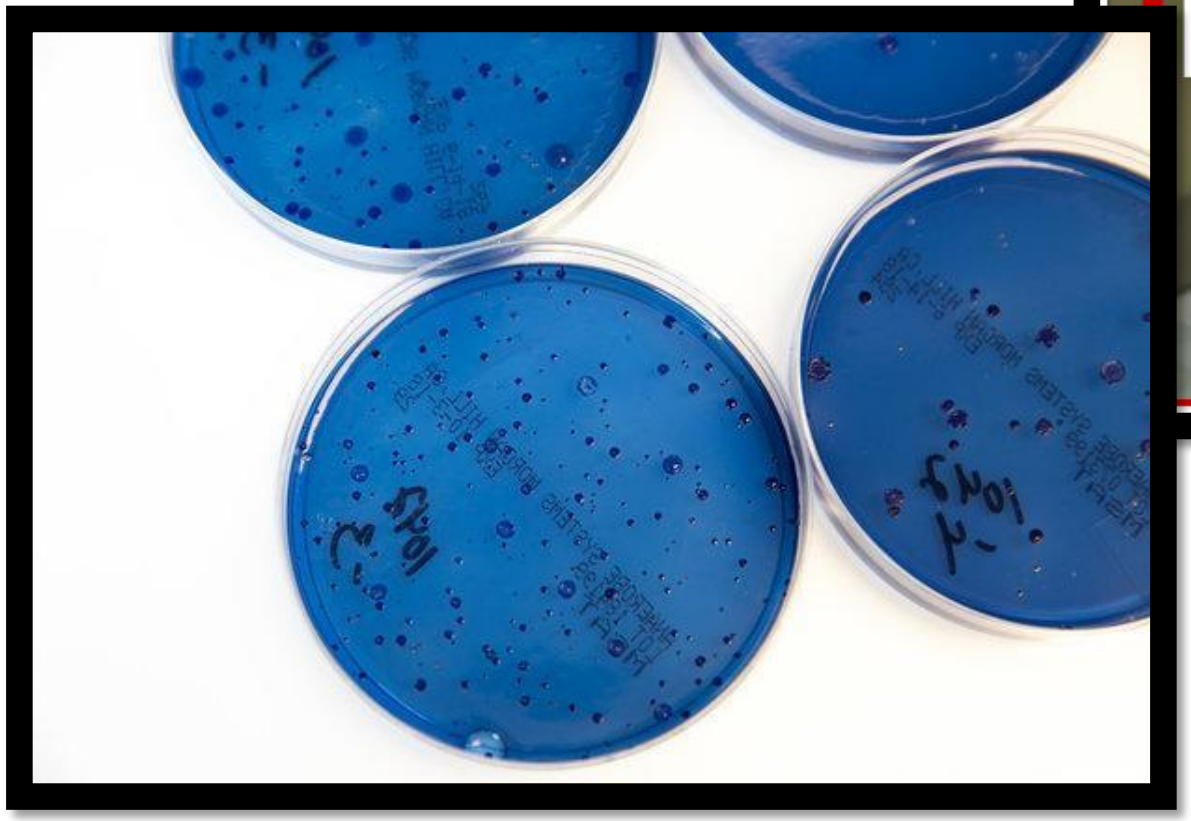
Transfaunation (transfer of fresh feces) from healthy horses to treat horses with diarrhea

rumen transfaunation: cows

1958: Dr. Eismann

FMT enema for 4 pts with pseudomembranous colitis (all recovered)

FMT (Fecal Microbiota Transplant)



Drug Companies and Doctors Battle Over the Future of Fecal Transplants- March 3,2019

Dietary Interventions in Cancer Reduction

International Journal of
Environmental Research and Public Health

MDPI

Review

Breast Cancer and Its Relationship with the Microbiota

Mariana F. Fernández [1,2,3,*], Iris Reina-Pérez [3], Juan Manuel Astorga [1], Andrea Rodríguez-Carrillo [1], Julio Plaza-Díaz [2,4,5] and Luis Fontana [2,4,5,*]

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check for updates

Abstract: The microorganisms that live symbiotically in human beings are increasingly recognized as important players in health and disease. The largest collection of these microorganisms is found in the gastrointestinal tract. Microbial composition reflects both genetic and lifestyle variables of the host. This microbiota is in a dynamic balance with the host, exerting local and distant effects. Microbial perturbation (dysbiosis) could contribute to the risk of developing health problems. Various bacterial genes capable of producing estrogen-metabolizing enzymes have been identified. Accordingly, gut microbiota is capable of modulating estrogen serum levels. Conversely, estrogen-like compounds may promote the proliferation of certain species of bacteria. Therefore, a crosstalk between microbiota and both endogenous hormones and estrogen-like compounds might synergize to provide protection from disease but also to increase the risk of developing hormone-related diseases. Recent research suggests that the microbiota of women with breast cancer differs from that of healthy women, indicating that certain bacteria may be associated with cancer development and with different responses to therapy. In this review, we discuss recent knowledge about the microbiome and breast cancer, identifying specific characteristics of the human microbiome that may serve to develop novel approaches for risk assessment, prevention and treatment for this disease.

Keywords: breast cancer; estrobolome; estrogens; microbiota

1. Introduction

The incidence of breast cancer (BC) worldwide has risen to unprecedented levels in recent decades, making it the major cancer of women in many parts of the world nowadays [1]. It is not only the most frequently diagnosed cancer (excluding non-melanoma skin cancers) among women worldwide, affecting one in eight women during their lifetime, but also one of the leading causes of cancer mortality in women, with more than 0.5 million deaths in 2012 (6.4% of total cancer deaths, globally, and 15.4% in more developed countries) [2,3]. In 2012, BC accounted for approximately 1.7 million new cases (25% of total cancer incidence, globally). Moreover, between 2008 and 2012 the incidence of BC increased by 20%, and mortality by 14% [4]. Rates are generally high in North America, Australia-New Zealand,

Breast Cancer and the Microbiome

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LITERATURE REVIEW Open Access

Breast Cancer and Diet

The Role of Diet and Lifestyle in Women with Breast Cancer: An Update Review of Related Research in the Middle East

Zainab Taha[1] and Sakina E. Eltom[2,3,*]

Abstract

Breast cancer is the most common malignancy among Arab women in Eastern Mediterranean Region (EMR). The incidence of breast cancer has substantially increased in recent years among this women population, especially those younger than 50, and the incidence is expected to double by 2030. Considerable experimental evidence supports the potential role of dietary habits and lifestyle in cancer etiology and cancer prevention. In this review we examined the literature for evidence to link dietary choices and the rise in incidence and mortality of breast cancer among women in EMR. A literature search was conducted in PubMed and Ovid MEDLINE databases up to December 2017. The search terms used are breast cancer prevalence, breast cancer incidence worldwide, breast cancer and: nutrition, protein intake, vitamin D intake, fat intake, phytoestrogens, EMR, Arab, Middle East, Gulf countries, the UAE Arab women, breast cancer risk, diet, and chemoprevention. We found evidence to suggest that there is an alarming epidemic of obesity among women in most of the EMR countries, especially Gulf Cooperation Council (GCC) countries. The rise in the new breast cancer cases among women could be attributed to excess body weight. Their dietary pattern, which correlates with obesity, can be an important factor in the etiology of cancer. Although very few studies were found to support a direct causal relationship between obesity and breast cancer in the EMR, circumstantial evidence clearly points to the possible role of the epidemic, obesity, in this population and the startling rise in cases of breast cancer. Well-designed and systematic studies are urgently needed to confirm these associations and to elucidate potential mechanisms. More urgently, calls to action are needed in many sectors and at all levels of society, to establish intensive strategies for reducing obesity and promoting an overall healthy diet. Continued and expanded research on diet, lifestyle, and breast cancer risk is urgently needed to build the foundation for future progress in evidence-based public health efforts.

Keywords: Arab women; breast cancer; chemoprevention; diet; Middle East; nutrition

Introduction

It is well documented that the risk factors for breast cancer are mainly related to hormones through their influence on growth of the mammary glands. The findings from the collaborative analysis of data that were collected from a total of 47 epidemiological studies conducted in 30 countries have contributed tremendously to shed light on factors that are associated with breast cancer. These findings were published by the Collaborative Group on Hormonal Factors in Breast Cancer and they have established an important role for childbearing and breastfeeding on breast cancer risk.[1] However, dietary factors can play a role in the etiology of breast cancer.

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The rise in the new breast cancer cases among women could be attributed to excess body weight. Their dietary pattern, which correlates with obesity, can be an important factor in the etiology of cancer.

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Anti-Inflammatory Diets

Am Coll Nutr. 2015;34 Suppl 1:14-21. doi: 10.1080/07315724.2015.1080105.

A diet rich in colorful, non-starchy vegetables can contribute adequate amounts of polyphenols to help inhibit nuclear factor (NF)-κB (primary molecular target of inflammation)

Understanding the impact of an anti-inflammatory diet on silent inflammation can elevate the status of diet from simply a source of calories to the cutting edge of gene-silencing technology.

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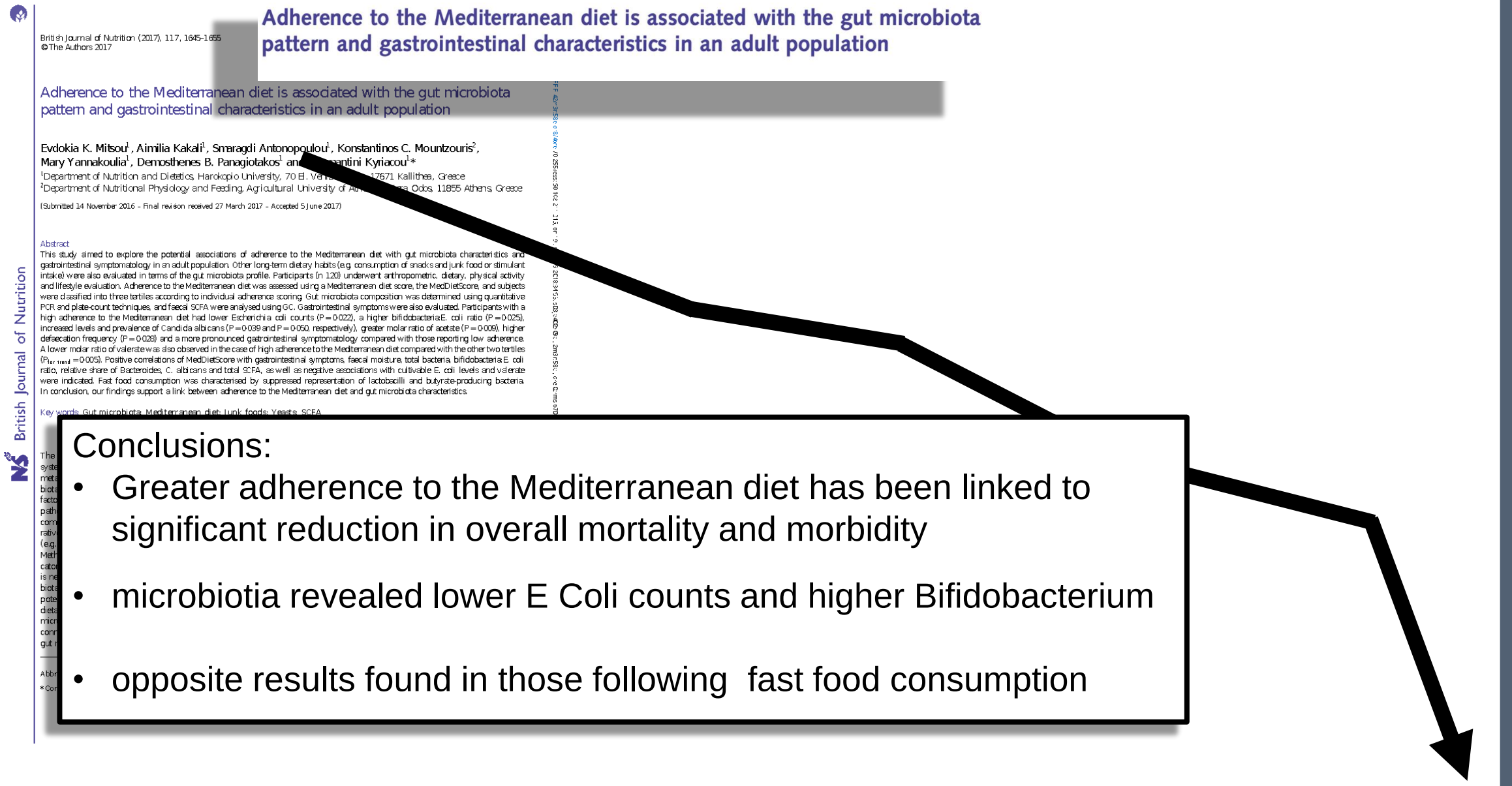

British Journal of Nutrition (2017), 117, 1645–1655
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Adherence to the Mediterranean diet is associated with the gut microbiota pattern and gastrointestinal characteristics in an adult population

Adherence to the Mediterranean diet is associated with the gut microbiota pattern and gastrointestinal characteristics in an adult population

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(Submitted 14 November 2016 – Final revision received 27 March 2017 – Accepted 5 June 2017)

Abstract
This study aimed to explore the potential associations of adherence to the Mediterranean diet with gut microbiota characteristics and gastrointestinal symptomatology in an adult population. Other long-term dietary habits (e.g. consumption of snacks and junk food or stimulant intake) were also evaluated in terms of the gut microbiota profile. Participants (n 120) underwent anthropometric, dietary, physical activity and lifestyle evaluation. Adherence to the Mediterranean diet was assessed using a Mediterranean diet score, the MedDietScore, and subjects were classified into three tertiles according to individual adherence scoring. Gut microbiota composition was determined using quantitative PCR and plate-count techniques, and faecal SCFA were analysed using GC. Gastrointestinal symptoms were also evaluated. Participants with a high adherence to the Mediterranean diet had lower Escherichia coli counts ($P = 0·022$), a higher bifidobacteria:E. coli ratio ($P = 0·025$), increased levels and prevalence of Candida albicans ($P = 0·039$ and $P = 0·050$, respectively), greater molar ratio of acetate ($P = 0·009$), higher defaecation frequency ($P = 0·028$) and a more pronounced gastrointestinal symptomatology compared with those reporting low adherence. A lower molar ratio of valerate was also observed in the case of high adherence to the Mediterranean diet compared with the other two tertiles ($P_{\text{for trend}} = 0·005$). Positive correlations of MedDietScore with gastrointestinal symptoms, faecal moisture, total bacteria, bifidobacteria:E. coli ratio, relative share of Bacteroides, C. albicans and total SCFA, as well as negative associations with cultivable E. coli levels and valerate were indicated. Fast food consumption was characterised by suppressed representation of lactobacilli and butyrate-producing bacteria. In conclusion, our findings support a link between adherence to the Mediterranean diet and gut microbiota characteristics.

Key words: Gut microbiota: Mediterranean diet: Junk foods: Yeasts: SCFA

British Journal of Nutrition

Conclusions:

- Greater adherence to the Mediterranean diet has been linked to significant reduction in overall mortality and morbidity
- microbiotia revealed lower E Coli counts and higher Bifidobacterium
- opposite results found in those following fast food consumption

Heme Iron from Meat and Risk of Colorectal Cancer: A Meta-analysis and a Review of the Mechanisms Involved

Published OnlineFirst January 5, 2011; DOI: 10.1158/19-

MiniReview

Heme Iron from Meat and Risk of Colorectal C
A Meta-analysis and a Review of the Mechanisms Involved

Nadia M. Bastide, Fabrice H.F. Pierre, and Denis E. Corpet

Abstract

Red meat and processed meat intake is associated with a risk of colorectal cancer, a major cause of death in affluent countries. Epidemiological and experimental evidence supports the hypothesis that heme iron present in meat promotes colorectal cancer. This meta-analysis of prospective cohort studies of colon cancer reporting heme intake included 566,607 individuals and 4,734 cases of colon cancer. The relative risk of colon cancer was 1.18 (95% CI: 1.06–1.32) for subjects in the highest category of heme iron intake compared with those in the lowest category. Epidemiological data thus show a suggestive association between dietary heme and risk of colon cancer. The analysis of experimental studies in rats with chemically-induced colon cancer showed that dietary hemoglobin and red meat consistently promote aberrant crypt foci, a putative precancer lesion. The mechanism is not known, but heme iron has a catalytic effect on (i) the endogenous formation of carcinogenic *N*-nitroso compounds and (ii) the formation of cytotoxic and genotoxic aldehydes by lipoperoxidation. A review of evidence supporting these hypotheses suggests that both pathways are involved in heme iron toxicity.

Cancer Prev Res; 4(2); 177–84. ©2011 AACR.

Introduction

Cancer of the colon and rectum, taken together, are the third most common type of cancer worldwide (1). In most publications, colon and rectal cancer are studied together and the term colorectal cancer (CRC) is used, which we also use here, except when the publications refer specifically to colon or rectal cancer. CRC is the second most common cause of cancer death in affluent countries. Dietary modifications might reduce this cancer burden by up to 70% (2). Three recent meta-analyses showed that total meat intake is not related to risk but that intake of red or processed meat is associated with a modest, but significant risk of CRC (3–5). Processed meat intake appears to be more closely linked with the risk of CRC than fresh red meat intake. In its 2007 report, the World Cancer Research Fund panel recommended that one should limit intake of red meat and avoid processed meat (1).

Several mechanisms may explain the relationship between the risk of CRC and the intake of red or pro

cessed meat. First, meat cooked at high
contains mutagenic heterocyclic amines. But
amines might not be major players in CRC
consumption of chicken is a major contribu
of heterocyclic amines, but is not associated
(6); and (ii) doses of heterocyclic amines
cancer in animals are 1,000 to 100,000 times
the dose ingested by humans (7). A secon
suggests that the high saturated fat conten
processed meat increases the risk of CRC
studies, including a recent meta-analysis,
effect of saturated fat on colorectal ca
(8–11). A third hypothesis concerns the
N-nitroso compounds (NOC), which can b
the gastrointestinal tract by N-nitrosation
derived amines or amides. The role of NO
cancer is discussed in the following text.
unlikely hypotheses involve the high protein
and salt content of red or processed meat. Fo
all these mechanisms, see ref. 12.

Sesink and colleagues suggested that heme
form of hemin [chloroprotoporphyrin IX iron
form of heme, may explain the link betwee
colon cancer and red meat intake, and the l
with white meat intake (13). Epidemiologica
mental evidence support heme toxicity. Hem
an iron atom present at the center of a large
organic ring called a porphyrin (Fig. 1). Hem
In so-called hemoprotein, that is, hemoglobi
(both involved in the oxygen supply), and in
(which catalyze electron transfer reactions

Authors' Affiliation: Université de Toulouse, INRA TOXALIM (Research Centre in Food Toxicology), INP ENVT, Toulouse, France

Note: Supplementary data for this article are available at Cancer Prevention Research Online (http://cancerprevres.aacrjournals.org/).

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doi: 10.1158/1940-6207.CAPR-10-0113

- CRC (Colo Rectal Cancer) is the third most common cancer worldwide
- Heme content in red meat is 10 times greater than that of white meat.
- N-nitroso compounds (NOCs) produced by bacterial decarboxylation of amino acids and lipid peroxidation create free radicals and increases carcinogenisis .

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Free Radical Exposure and Cancer Development

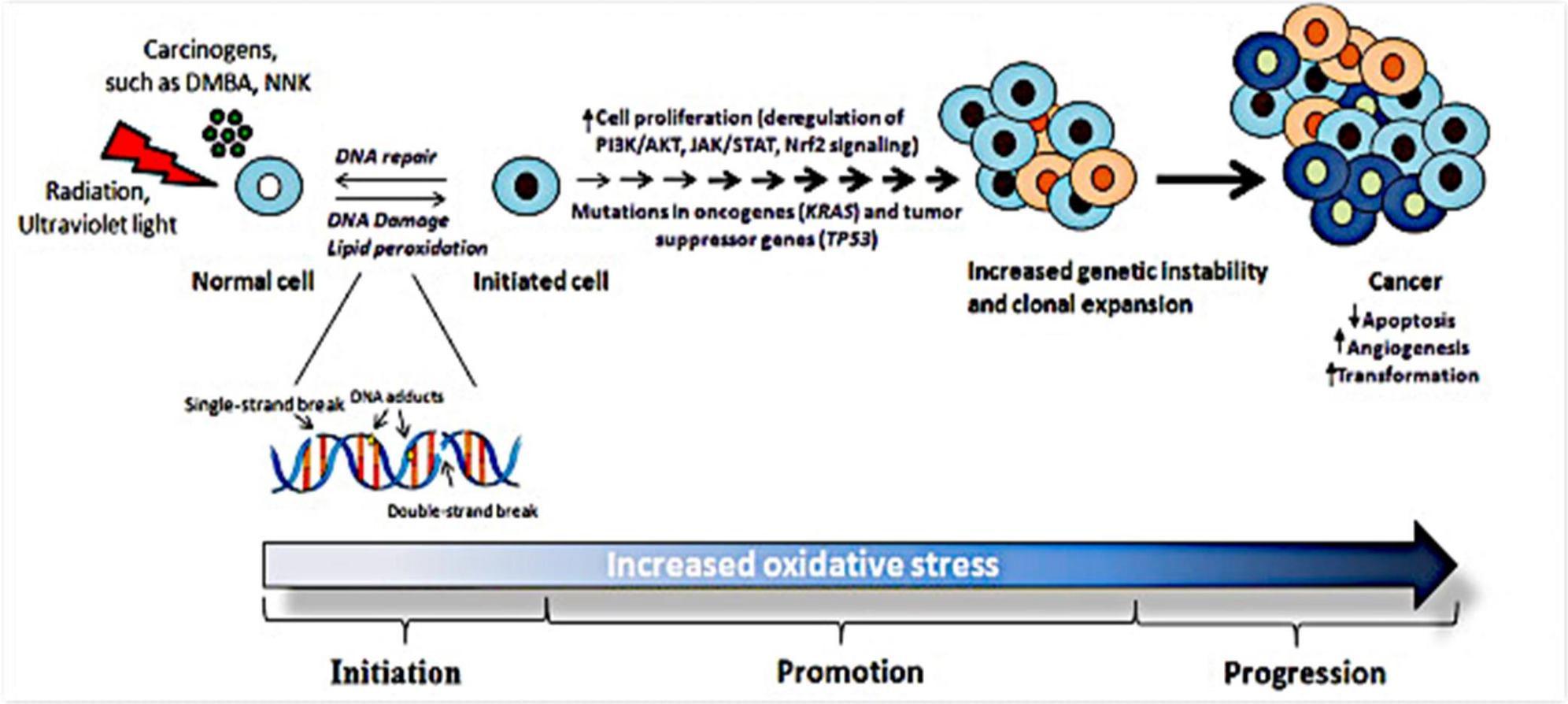
Hydroxyl Radical (0H)

- Extremely reactive if generated in the area of DNA- breaks strands

Superoxide 02 interacts with Nitric Oxide (NO)

- Interacts with protein and causes cell damage

Relationships between Oxidative Stress, Cancer Development and Therapeutic Interventions



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Examples of Anti-oxidants:

Flavonoids and Cancer Prevention: A Review of the Evidence

Published online, *13 Aug 2012, Authors: Donato F. Romagnolo PhD, MS & Ornella I. Selmin PhD*

Epidemiological studies suggest dietary intake of flavonoids may reduce the risk of tumors of the breast, colon, lung, prostate, and pancreas

A Major Challenge

Dose and timing of exposure may influence the anticancer response to flavonoid-rich diets. A limited number of intervention trials of flavonoids have documented cancer preventative effects. Proposed anticancer mechanisms for flavonoids are: inhibition of proliferation; inflammation; invasion; metastasis; and activation of apoptosis.

Vitamin C

Vitamin C is a commonly used water-soluble vitamin. Although many mammals can produce vitamin C, humans must obtain vitamin C from foods and other sources.

- Involved in tyrosine metabolism and is a cofactor in the synthesis of carnitine, thyroxin, norepinephrine, dopamine, and tryptophan.
- Vitamin C metabolic processes includes oxidation-reduction reactions and cellular respiration, carbohydrate metabolism, synthesis of lipids and proteins, catabolism of cholesterol to bile acids, conversion of folic acid to folinic acid, and iron metabolism.
- Vitamin C deficiency can cause fatigue, personality changes, and decline in psychomotor performance and motivation within 84 to 97 days.

Vitamin C

Vitamin C is a commonly used water-soluble vitamin. Although many mammals can produce vitamin C, humans must obtain vitamin C from foods and other sources.

- Hydrogen peroxide is a pro-oxidant, capable of causing free radical damage.
- In normal cells, the enzyme, ***catalase*** disables hydrogen peroxide. Thus, in normal cells, vitamin C retains its antioxidant effect.
- Tumor cells, however, *lack* ***catalase***, and cancers are thus vulnerable to damage from hydrogen peroxide.

Vitamin C

Vitamin C is a commonly used water-soluble vitamin. Although many mammals can produce vitamin C, humans must obtain vitamin C from foods and other sources.

- Tumor cells also selectively take up vitamin C, so they accumulate it to higher levels than normal cells, increasing their vulnerability to hydrogen peroxide.
- High doses can be harmless (or even beneficial) to normal cells, but at the same time, kill tumor cells.
- Furthermore, since IV C creates a pro-oxidant effect, it is unlikely to counteract the effect of chemotherapy.

Further Vitamin C Studies

High Doses of Vitamin C to Improve Cancer Treatment Passes Human Safety Trial

Cell Press, March 30, 2017

High-Dose Parenteral Ascorbate Enhanced Chemosensitivity of Ovarian Cancer and Reduced Toxicity

Science News. *Authors: Yan Ma, Julia Chapman, Mark Levine, Kishore Polireddy, JeanneDrisko and Qi Chen*

Intravenous Vitamin C Administration Improves Quality of Life in Breast Cancer Patients during Chemo-/Radiotherapy and Aftercare: Results of a Retrospective, Multicentre, Epidemiological Cohort Study in Germany

In Vivo, *2011 Nov-Dec;25(6):983-90Authors: Claudia Vollbracht, Berthold Schneider, Van Leendert, Gabrielle Weiss, LeoAuerbach, Josef Beuth*

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Turmeric

The applicable part of turmeric is the rhizome. Turmeric's major active constituents are curcuminoids including curcumin (diferuloylmethane), a yellow pigment used as a food coloring

- Curcumin seems to have anti-inflammatory activity, possibly by inhibiting cyclooxygenase-2 (COX-2), prostaglandins, leukotrienes, and other cytokines involved in proinflammatory signaling pathways.
- Turmeric also exhibits chemopreventive and growth inhibitory activity against several tumor cell lines. It seems to induce apoptosis in cancer cells and may inhibit angiogenesis.
- Curcumin might reduce activity of procarcinogenic eicosanoids, such as prostaglandin-E2 and 5-hydroxyeicosatetraenoic acid (5-HETE), via inhibition of cyclooxygenases and 5-lipoxygenase

Turmeric

The applicable part of turmeric is the rhizome. Turmeric's major active constituents are curcuminoids including curcumin (diferuloylmethane), a yellow pigment used as a food coloring

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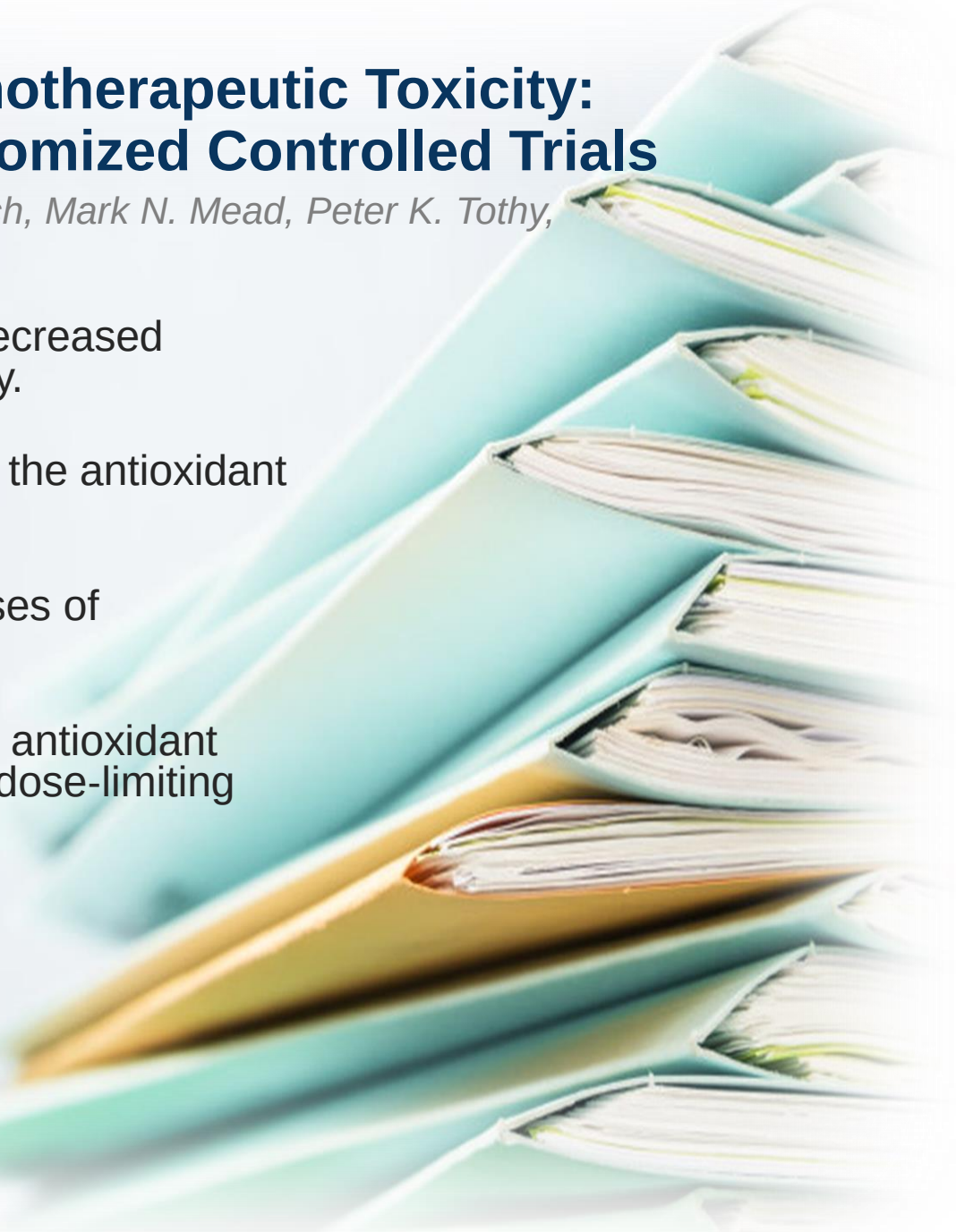
- Preliminary evidence suggests curcumin can also reduce precancerous rectal aberrant crypt foci. Curcumin might have antithrombotic effects. Preliminary research suggests it might inhibit platelet-activating factor and arachidonic acid platelet aggregation, possibly by interfering with thromboxane synthesis.
- Other preliminary research suggests that turmeric and curcumin might also have antioxidant and immunostimulatory effects.

Impact of Antioxidant Supplementation on Chemotherapeutic Toxicity: A Systematic Review of the Evidence from Randomized Controlled Trials

IJC International Journal of Cancer, *Authors: Keith I Block, Amanda C. Koch, Mark N. Mead, Peter K. Tothy, Robert A. Newman, Charlotte Gyllenhaal*

- The majority (24) of the 33 studies included reported evidence of decreased toxicities from the concurrent use of antioxidants with chemotherapy.
- Only 1 study (vitamin A) reported a significant increase in toxicity in the antioxidant group.
- Five studies reported the antioxidant group completed more full doses of chemotherapy or had less dose reduction than control groups.
- This review provides the first systematically reviewed evidence that antioxidant supplementation during chemotherapy holds potential for reducing dose-limiting toxicities.

Literature suggests that up to 87% of patients with cancer take antioxidant supplements.



Hyperbaric Oxygen Therapy

Hyperbaric Oxygen Therapy (HBOT)

Cancer and Hyperbaric

Hyperbaric oxygen therapy (HBOT) is currently being utilized in conjunction with conventional treatments, including radiation and chemotherapy. Cancer thrives in hypoxic environments and HBOT has been shown to increase these oxygen levels to weaken tumors and reduce their aggressiveness. Studies have demonstrated the benefits of HBOT for cancer with the following:

Enhance “Conventional” Cancer Therapies and Treatments with HBOT

- Reduce Tumor Hypoxia
- Better Radiation Therapy Results
- Improves Chemotherapy Outcome
- Enhances Brain Treatment
- Decreases Tumor Drug Resistance
- Allows for Optimal Therapy Dosage to be Attained
- Increases Post-Op Fibroblast Activation

Reduce Side Effects of “Conventional” Cancer Therapies and Treatment with HBOT

- Reduces Radiation Therapy Side Effects
- Decreases Chemotherapy Side Effects
- Accelerates Post-Operative Healing & Prevents Infection
- Reduces Chemo-Brain Syndrome Symptoms

Enhance IV Cancer Treatments with HBOT

- Increase Intravenous Vitamin C Therapy Effects
- Enhance Chemotherapy Uptake

Reduce Tumor Aggressiveness with HBOT

- Weakens Hypoxic Tumors
- Targets Metastatic Tumors

Increase Natural Killer Cell Activity with HBOT

- Increase Oxy-Radical Production
- Amplifies Apoptosis Effect

Acupuncture

Helps subdue the Pain from conventional Cancer treatments

Services

63%

OF CANCER PATIENTS EXHIBITED POSTIVE RESULTS

Up to 31%

of patients Use Accupunctrue

Acupuncture

Acupuncture for Cancer-Related Fatigue in Patients With Breast Cancer: A Pragmatic Randomized Controlled Trial

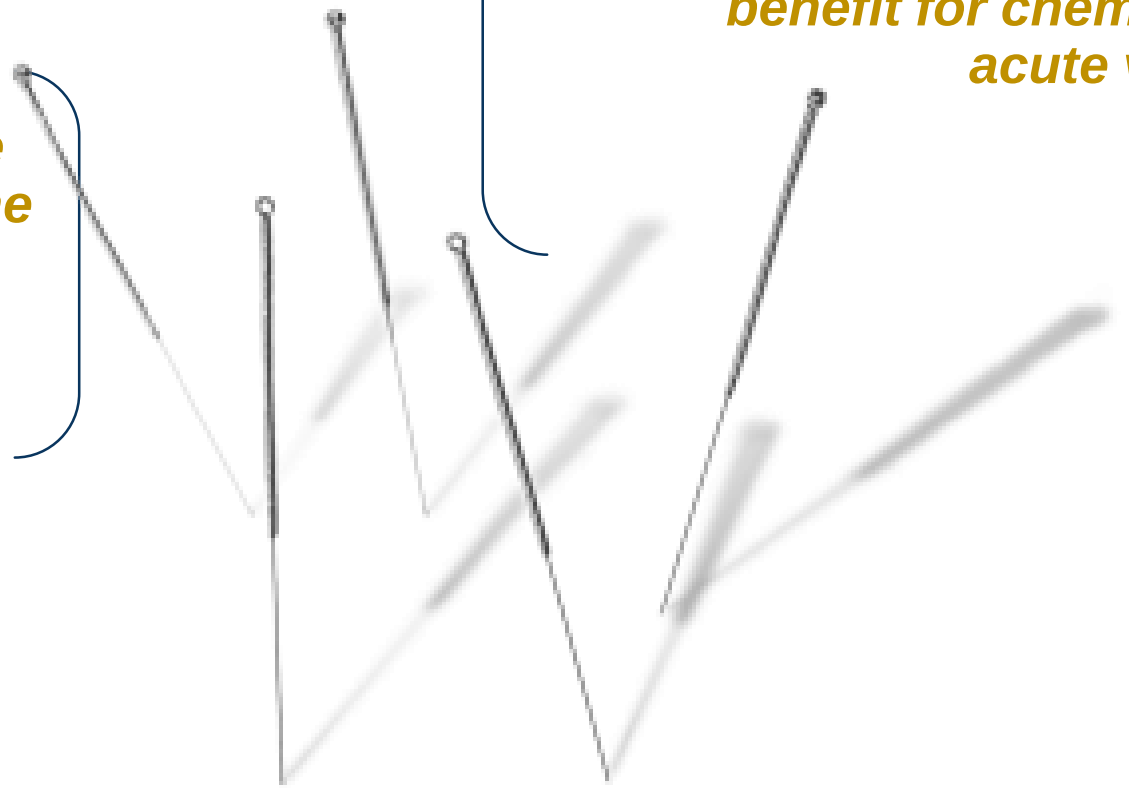
Journal of Clinical Oncol 30:4470-4476 *Alexander Molassiotis, Joy Bardy, et al.*

Acupuncture is an effective intervention for managing the symptom of cancer related fatigue and improving patients' quality of life

Acupuncture-Point Stimulation for Chemotherapy-Induced Nausea and Vomiting

Cochrane Database Syst. Rev. *2006 Apr 19, Ezzo JM1, Richardson MA, Vickers A, Allen C, et al.*

Electroacupuncture has demonstrated benefit for chemotherapy-induced acute vomiting



Stram Center for Integrative Medicine

Real-Life Application

Case Presentation

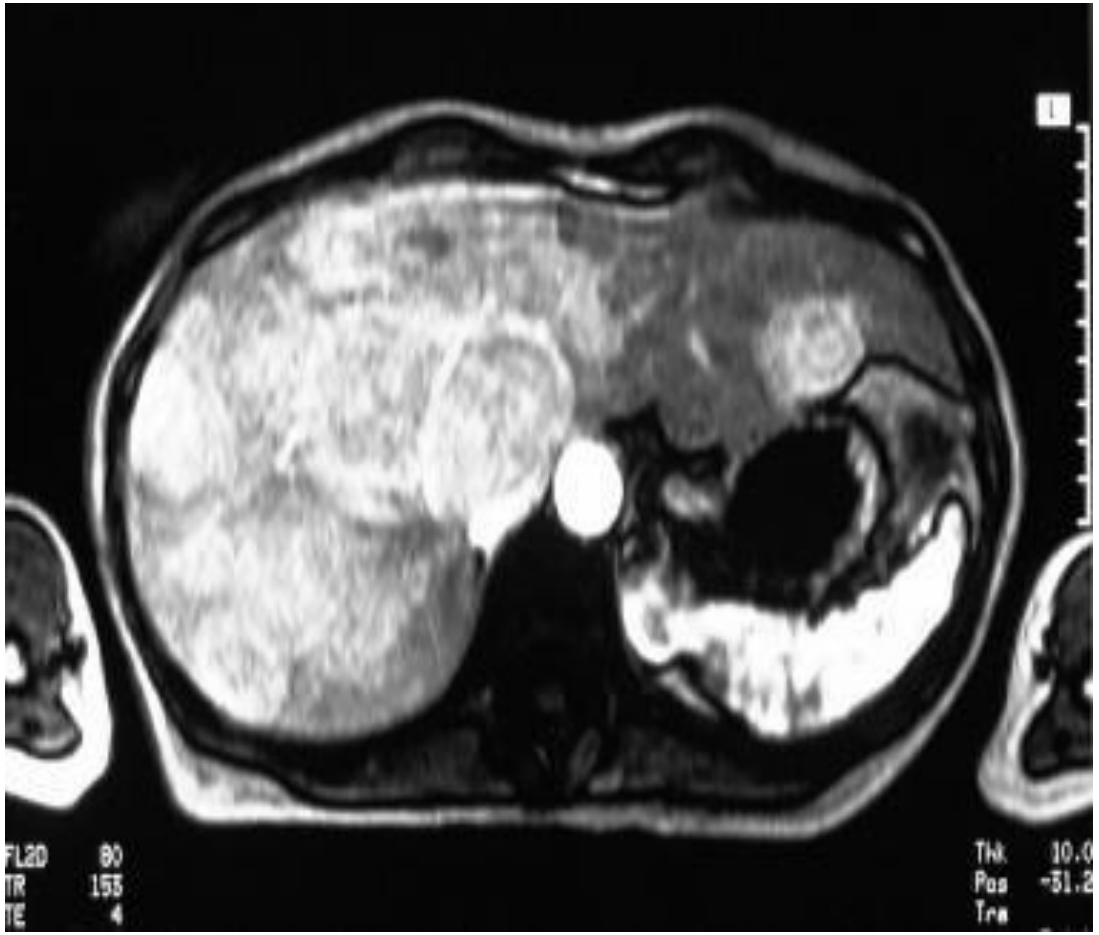
- Patient was tested in early twenties as part of a research study. Patient + BRCA 2.
- October 2005- DCIS- s/p right breast lumpectomy s/p radiation- completed 6 weeks.
- July 2015- had mammogram- patient developed lump in left breast and chose to have a double mastectomy with implants . All biopsies have been ER +. No chemotherapy or radiation at this time. Patient reports she has never had hormone therapy.
- August 2018- patient saw PCP and had blood work and was called immediately and advised to go to the hospital. Patient reports "something about a C-protein and concern for infection and anemia". Patient also had a chest x-ray that also made PCP concerned. Patient was told she had stage IV metastatic breast cancer to bones (spine, pelvis, sternum and ribs). Patient reports blood count was 9.0 and her recent blood work revealed 7.8.

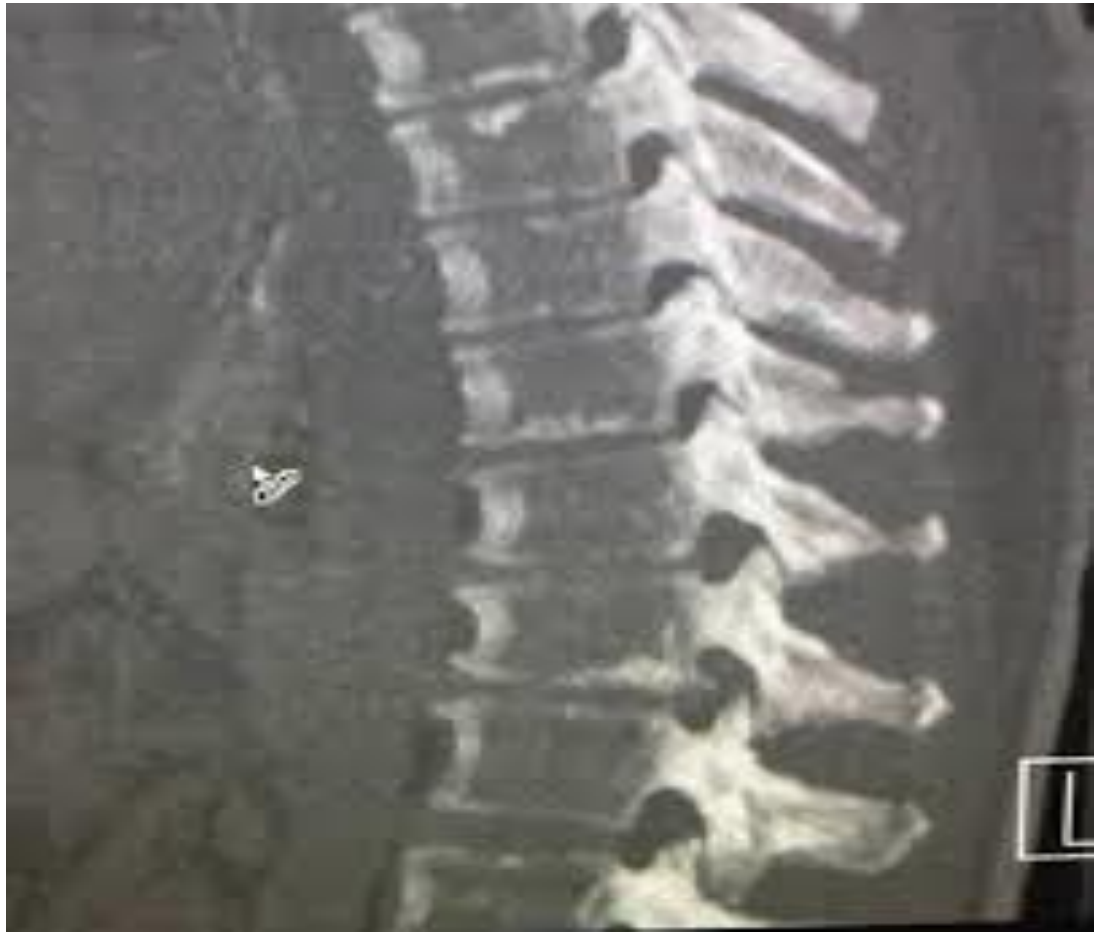
Symptoms

Most prominent symptom:

- Generalized pain
  Intensity: 7/10 (10=worst), it can go down to 3/10
  Frequency: Daily
- Ambulating with a walker because it makes her more comfortable.

Images Representing Metastasis





Specimen ID: 269-381-0255-0
Control ID: 0000137926

Acct #: 31504485 Phone: (518) 689-2244 Rte: 11

[redacted]

Ronald Stram MD
90 Adams Place
DELMAR NY 12054

Patient Details
DOB: 11/09/1972
Age(y/m/d): 045/10/17
Gender: F SSN:
Patient ID: 31504485.15841

Specimen Details
Date collected: 09/26/2018 1116 Local
Date received: 09/26/2018
Date entered: 09/26/2018
Date reported: 10/03/2018 1626 ET

Physician Details
Ordering: M SANDERSON
Referring:
ID:
NPI: 1245789783

General Comments & Additional Information
Alternate Control Number: 0000137926 **Alternate Patient ID:** 31504485.15841

Ordered Items
Helper/Suppress/Natural Killer; Comp. Metabolic Panel (14); G-6-PD, Quant, Blood and RBC; Vitamin B12 and Folate; Vitamin D, 1,25 + 25-Hydroxy; Methylmalonic Acid, Serum; Cortisol; Vitamin B6, Plasma; VEGF, Serum; C-Reactive Protein, Cardiac; CA 27.29; Tumor Necrosis Factor-Alpha; Interleukin-2, Serum; Interleukin-6, Serum; Interleukin-8, Serum; IL-2 Receptor Alpha; MTHFR; Sedimentation Rate-Westergren; Fibrinogen Activity; Immunoglobulin G, Qn, Serum; Ferritin, Serum; Calcium, Ionized, Serum; Magnesium, RBC; Request Problem

TESTS	RESULT	FLAG	UNITS	REFERENCE INTERVAL	LAB
Helper/Suppress/Natural Killer					
% NK (CD56/16)	9.6		%	1.4 - 19.4	01
Ab NK (CD56/16)	106		/uL	24 - 406	
Absolute CD 3	890		/uL	622 - 2402	
Absolute CD 4 Helper	650		/uL	359 - 1519	
Abs. CD 8 Suppressor	233		/uL	109 - 897	
% CD 3 Pos. Lymph.	80.9		%	57.5 - 86.2	01
% CD 4 Pos. Lymph.	**59.1**	**High**	%	30.8 - 58.5	01
% CD 8 Pos. Lymph.	21.2		%	12.0 - 35.5	01
CD4/CD8 Ratio	2.79			0.92 - 3.72	
WBC	6.7		x10E3/uL	3.4 - 10.8	01
RBC	**3.49**	**Low**	x10E6/uL	3.77 - 5.28	01
Microcytes present.					
Anisocytosis present.					
Hemoglobin	**8.6**	**Low**	g/dL	11.1 - 15.9	01
Hematocrit	**28.0**	**Low**	%	34.0 - 46.6	01
MCV	80		fL	79 - 97	01
MCH	**24.6**	**Low**	pg	26.6 - 33.0	01
MCHC	**30.7**	**Low**	g/dL	31.5 - 35.7	01
RDW	**22.9**	**High**	%	12.3 - 15.4	01
Platelets	**410**	**High**	x10E3/uL	150 - 379	01
Platelet count verified by examination of peripheral blood smear.					
Large platelets were observed.					
Neutrophils	60		%	Not Estab.	01
Lymphs	17		%	Not Estab.	01
Monocytes	9		%	Not Estab.	01
Eos	1		%	Not Estab.	01
Basos	0		%	Not Estab.	01

[redacted] Patient ID: 31504485.15841 Control ID: 0000137926

Specimen ID: 269-381-0255-0
Date collected: 09/26/2018 1116 Local

TESTS	RESULT	FLAG	UNITS	REFERENCE INTERVAL	LAB
multiple tests. The requested testing requires a separate specimen for each test requested.					
R/D Systems Quantikine Enzyme Immunoassay (EIA)					
Results of this test are labeled for research purposes only by the assay's manufacturer. The performance characteristics of this assay have not been established by the manufacturer. The result should not be used for treatment or for diagnostic purposes without confirmation of the diagnosis by another medically established diagnostic product or procedure. The performance characteristics were determined by LabCorp.					
C-Reactive Protein, Cardiac	**116.74**	**High**	mg/L	0.00 - 3.00	01
Results confirmed on dilution.					
Relative Risk for Future Cardiovascular Event					
Low				**<1.00**	
Average				**1.00 - 3.00**	
High				**>3.00**	
CA 27.29	**688.8**	**High**	U/mL	0.0 - 38.6	01
Specimen was diluted in order to obtain results.					
Results were repeated.					
Bayer Centaur/ACS methodology					
Values obtained with different assay methods or kits cannot be used interchangeably. Results cannot be interpreted as absolute evidence of the presence or absence of malignant disease.					
Tumor Necrosis Factor-Alpha					
Tumor Necrosis Factor-Alpha				0.0 - 2.2	02
Test Not Performed. One specimen was submitted with requests for multiple tests. The requested testing requires a separate specimen for each test requested.					
Comment:					02
Results of this test are labeled for research purposes only by the assay's manufacturer. The performance characteristics of this assay have not been established by the manufacturer. The result should not be used for treatment or for diagnostic purposes without confirmation of the diagnosis by another medically established diagnostic product or procedure. The performance characteristics were determined by LabCorp.					
Interleukin-2, Serum	**<31.2**		**pg/mL**	**0.0 - 31.2**	**02**
Results for this test are for research purposes only by the assay's manufacturer. The performance characteristics of this product have not been established. Results should not be used as a diagnostic procedure without confirmation of the diagnosis by another medically established diagnostic product or procedure.					
Interleukin-6, Serum	**30.5**	**High**	**pg/mL**	**0.0 - 15.5**	**02**

[redacted] Patient ID: 31504485.15841 Control ID: 0000137926 Specimen ID: 269-381-0255-0 Date collected: 09/26/2018 1116 Local

TESTS	RESULT	FLAG	UNITS	REFERENCE INTERVAL	LAB
Results for this test are for research purposes only by the assay's manufacturer. The performance characteristics of this product have not been established. Results should not be used as a diagnostic procedure without confirmation of the diagnosis by another medically established diagnostic product or procedure.					
Interleukin-8, Serum	50.6		pg/mL	0.0 - 66.1	02
Results for this test are for research purposes only by the assay's manufacturer. The performance characteristics of this product have not been established. Results should not be used as a diagnostic procedure without confirmation of the diagnosis by another medically established diagnostic product or procedure.					
IL-2 Receptor Alpha					
IL-2 Receptor Alpha	**1580**	**High**	U/mL	223 - 710	02
Comment:					02
Results of this test are labeled for research purposes only by the assay's manufacturer. The performance characteristics of this assay have not been established by the manufacturer. The result should not be used for treatment or for diagnostic purposes without confirmation of the diagnosis by another medically established diagnostic product or procedure. The performance characteristics were determined by LabCorp.					
MTHFR					
MTHFR, DNA Analysis					
Result: A1298C/A1298C					03
Two copies of the same mutation (A1298C/A1298C) identified					
Interpretation:					
This individual is homozygous for the MTHFR A1298C variant (two copies). The MTHFR C677T variant was not identified. This MTHFR result is not associated with an increased risk of hyperhomocysteinemia, venous thrombosis, coronary artery disease, or recurrent pregnancy loss. However, hyperhomocysteinemia may also occur due to mutations in enzymes other than MTHFR that are involved in homocysteine metabolism, or arise due to acquired factors. In the evaluation of vascular and obstetric risk, consider measuring fasting homocysteine. Other risk factors may be detected through systematic clinical laboratory analysis.					
Please Note:					03
Methylenetetrahydrofolate reductase (MTHFR) is a key enzyme in the folate pathway and is responsible for the metabolism of homocysteine. There are two common variants in the MTHFR gene, c.655c>T (p.Ala222Val), referred to as C677T, and c.1286A>C (p.Glu429Ala), referred to as A1298C. Individuals homozygous for C677T (two copies of the variant), have decreased activity of the MTHFR enzyme and a predisposition to hyperhomocysteinemia, particularly when deficient in folate. Hyperhomocysteinemia is a risk factor for venous thrombosis and coronary artery disease and is associated with an increased risk of fetal open neural tube defects. The C677T variant does not independently increase risk of these conditions in the absence of hyperhomocysteinemia. The A1298C variant is not associated with					

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TESTS	RESULT	FLAG	UNITS	REFERENCE INTERVAL	LAB
elevated homocysteine levels unless a C677T variant is also present; however, the clinical significance of heterozygosity for both C677T and A1298C is controversial. Population data suggest that these two variants are not present on the same chromosome, but rare exceptions have been reported of triple variant MTHFR genotypes (ie. homozygous for one variant and heterozygous for the other). Homozygosity for C677T has an estimated frequency of 10% to 15% in Caucasians and 25% in Hispanics.					
Additional information:					
Dietary folic acid, B6 and B12 supplementation has been suggested to lower homocysteine levels in some people. Folic acid supplementation has been shown to reduce the occurrence of neural tube defects. Genetic counselors are available for health care providers to discuss results at 1-800-345-GENE.					
Methodology:					
DNA analysis of the MTHFR gene was performed by PCR amplification followed by restriction analysis. The diagnostic sensitivity is >99% for both. Molecular-based testing is highly accurate, but as in any laboratory test, rare diagnostic errors may occur. All test results must be combined with clinical information for the most accurate interpretation.					
This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration.					
References:					
Botto LD, Yang Q. Am J Epidemiol 2000; 151(9):862-877.					
Eldibany MM, Caprini JA. Arch Pathol Lab Med 2007; 131(6):872-884.					
Frosst P et al. Nat Genet 1995; 10(1):111-113.					
Hickey SE et al. Genet Med 2013; 15(2):153-156.					
Lockwood C et al. Obstet Gynecol 2011; 118(3):730-740.					
Simone B et al. Eur J Epidemiol 2013; 28(8):621-647.					
Chevonne Eversley, PhD, FACMG					
Melissa A Hayden, PhD, FACMG					
Annette K Taylor, M.S., PhD, FACMG					
Alecia Willis, PhD, FACMG					
Hongli Zhan, PhD, FACMG					
Joseph B Kearney, PhD, FACMG					
Sedimentation Rate-Westergren	**75**	**High**	mm/hr	0 - 32	01
Fibrinogen Activity	**648**	**High**	mg/dL	193 - 507	01
Immunoglobulin G, Qn, Serum	726		mg/dL	700 - 1600	01
Ferritin, Serum	**1529**	**High**	ng/mL	15 - 150	01
Calcium, Ionized, Serum	4.9		mg/dL	4.5 - 5.6	01
Magnesium, RBC	5.9		mg/dL	4.2 - 6.8	02

Treatment Plan

Supplements

- Melatonin
- Collagen Peptides
- Methyl Factors
- Iron Bisglycinate
- MRS Mushroom Formula
- Turkey Tail
- ProEPA
- Turmeric

Adjunct Therapy

- Acupuncture
- IV Vitamin C 50 g 2x per week
- Hyperbaric Oxygen with a total of 40 sessions

Stram Center for Integrative Medicine

Quest Diagnostics

Report Status: Final

DIVIRGILIO, DANAY

Patient Information	Specimen Information	Client Information
[redacted]	Specimen: RK615975 Requisition: T432390001628 Collected: 01/11/2019 / 07:00 EST Received: 01/12/2019 / 02:45 EST Reported: 01/17/2019 / 15:45 EST	Client #: 43239 1000 SANDERSON, MEAGHAN STRAM CENTER 90 ADAMS PLACE DELMAR, NY 12054

Test Name	In Range	Out Of Range	Reference Range	Lab
IRON,TOTAL	111		40-190 mcg/dL	TBR
SED RATE,MOD WESTERGREN		34 H	< OR = 20 mm/h	TBR
VITAMIN B12		>2000 H	200-1100 pg/mL	TBR
CA 125	24		<35 U/mL	TBR

This test was performed using the Beckman Coulter chemiluminescent method. Values obtained from different assay methods cannot be used interchangeably. CA125 levels, regardless of value, should not be interpreted as absolute evidence of the presence or absence of disease.

C-REACTIVE PROTEIN (CRP)				TBR
C-REACTIVE PROTEIN	3.8		<8.0 mg/L	
INTERLEUKIN 6,HIGHLY SENS	4.75		0.31-5.00 pg/mL	QNI

This test was performed using a kit that has not been cleared or approved by the FDA. The analytical performance characteristics of this test have been determined by Quest Diagnostics Nichols Institute San Juan Capistrano. This test should not be used for diagnosis without confirmation by other medically established means.

INTERLEUKIN 2 (IL-2)	<38		LESS THAN 38 pg/mL	QNI

To convert pg/mL IL-2 to NIBSC units (U/mL), multiply the pg/mL value reported by 0.026. This assay was performed using the Endogen Human IL-2 ELISA kit.

This test was performed using a kit that has not been cleared or approved by the FDA. The analytical performance characteristics of this test have been determined by Quest Diagnostics Nichols Institute San Juan Capistrano. This test should not be used for diagnosis without confirmation by other medically established means.

VEGF,ELISA				QNI
VASCULAR ENDOTHELIAL GF		94 H	31-86 pg/mL	

This test was performed using a kit that has not been cleared or approved by the FDA. The analytical performance characteristics of this test have been determined by Quest Diagnostics Nichols Institute San Juan Capistrano. This test should not be used for diagnosis without confirmation by other medically established means.

TUMOR NECROSIS FACT-ALPHA				QNI
TNF-ALPHA,HIGHLY SENSITIVE	0.91		0.56-1.40 pg/mL	

TNF-alpha is not to be used as a diagnostic procedure without confirmation of the diagnosis by another established product or procedure.

The reference range is intended to be used for blood samples only. Reference ranges for body fluids other than blood have not been established.

This test was performed using a kit that has not been

Quest Diagnostics

Report Status: Final

DIVIRGILIO, DANAY

Patient Information	Specimen Information	Client Information
[redacted]	Specimen: RK615975 Collected: 01/11/2019 / 07:00 EST Received: 01/12/2019 / 02:45 EST Reported: 01/17/2019 / 15:45 EST	Client #: 43239 SANDERSON, MEAGHAN

Test Name	In Range	Out Of Range	Reference Range	Lab

cleared or approved by the FDA. The analytical performance characteristics of this test have been determined by Quest Diagnostics Nichols Institute San Juan Capistrano. This test should not be used for diagnosis without confirmation by other medically established means.

INTERLEUKIN 8	<5		<=5 pg/mL	ARU

INTERPRETIVE INFORMATION: Cytokines
Results are used to understand the pathophysiology of immune, infectious, or inflammatory disorders, or may be used for research purposes.

Test developed and characteristics determined by ARUP Laboratories. See Compliance Statement B: aruplab.com/CS

PERFORMING SITE:

ARU A.R.U.P., 500 Chipeta Way, Salt Lake City, UT 84108 Laboratory Director: Julio C. Delgado M.D M.S., CLIA: 46D0523979
QNI Quest Diagnostics, Nichols Institute, 33608 Ortega Highway, San Juan Capistrano, CA 92675 Laboratory Director: Irina Maranuca MD, CLIA: 05D0643352
TBR Quest Diagnostics, One Malcolm Avenue, Teterboro, NJ 07608 Laboratory Director: Lawrence Tsao, M.D., CLIA: 31D0696246

Questions