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Global Nutrition Research: Nutrition and Breast Cancer Prevention as a Model

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Abstract

The gene-environment interaction is paramount in light of the worldwide rise of incidence of chronic diseases, with cancers in the pole position. Diet is an environmental factor with potential to influence cancer onset by shaping the epigenome (i.e., the genome organization that controls the differential expression of genes). Yet, there is no consensus regarding how diet might help prevent breast cancer, the second most frequent malignancy globally. We propose that the complexity of breast cancers requires working on a global and multidisciplinary scale to further understand the relationship between breast cancer type, diet and the epigenome. This approach is the basis for the International Breast Cancer & Nutrition (IBCN) initiative and related symposia that gather scientists and clinicians from different backgrounds and world regions. A global endeavor will not only bring the diversity necessary to pinpoint important diet-gene relationships, it will also provide momentum to develop the models, detection and assessment tools, and funding and public policy framework necessary to advance primary prevention research for the benefit of all populations affected by breast cancer. This paradigm can be adapted to understanding diet-gene relationships for other chronic diseases.

Keywords

epigenome; primary prevention; dietary pattern; global health; chronic disease

Introduction

Nutrition as it relates to disease has not been rigorously investigated from a global perspective. Our vision of the world has changed over the past decade, particularly when it comes to health. Endeavors have shifted from single viewpoints on public health issues to international task forces that produce global recommendations. Consequently, nutrition guidelines to support health on earth (i.e., globally) exist,^{1, 2} yet the role of nutrition in the etiology of disease is being studied primarily from local perspectives. Even when large cohorts have been created to represent diverse populations, the scope is usually no more than a few countries on one continent. Such examples include the European Prospective Investigation into Cancer and Nutrition (EPIC) program³ and populations who have

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migrated from one continent to another e.g., Asian migrants to Hawaii and the West Coast studied for cancer development.⁴⁻⁵

Much work has been spent on studying dietary deficiencies in developing countries but these efforts mostly relate to the fight against communicable diseases (e.g., AID related projects⁶) and survival at birth and during childhood.⁷⁻⁸ However, cancer numbers have been slowly escalating until they have become a major threat for the populations. Therefore, in addition to high income countries where cancer burden has been a major concern for years, according to the World Health Organization (W.H.O.) cancer is the next catastrophic affliction in many low and middle income (LMI) countries.⁹⁻¹⁰ This threat is partly based on the lack of funds and infrastructure in many LMI countries to treat this disease. Consequently, emphasis ought to be placed on research aimed at primary prevention of cancer, i.e., to identify means to inhibit disease development when a risk exists. The need for primary prevention has become global. This is where nutrition could play a critical role.

Cancers of the colon, rectum, prostate, oral cavity, larynx, pharynx, esophagus, stomach, liver, pancreas, uterus, endometrium, kidney and breast are those listed by W.H.O. as influenced by nutrition.^{11; 9} According to W.H.O., 30% of cancers might be linked to dietary factors in industrialized countries, and the proposed rate of 20% for LMI countries might increase rapidly.⁹ General dietary recommendations linked to primary prevention by acting on nutrition include decreasing overweight in the population for most cancers, increasing fiber consumption for colon cancer, limiting alcohol consumption for breast and esophageal cancers, experiencing only moderate consumption of fermented salted food and salt preserved food for nasopharyngeal and stomach cancers and preserved meat for colorectal cancers.⁹ However, for breast cancer, which ranks first globally among cancers in terms of estimated age-standardized incidence,¹² there are many reports involving dietary patterns and specific dietary factors in the onset of the disease beside the risks associated with being overweight after menopause and alcohol consumption.¹³ Yet meta-analyses failed to identify specific aspects of the diet on which to focus due to the high variability in experiment design, the inability to compare studies and the lack of diversity in dietary patterns for a given analysis.¹⁴ An increasing number of studies that report growing breast cancer incidence in certain populations also point out a parallel between this rise and a change in dietary habits.^{15;16;17} Risk factors recognized thus far for breast cancer¹⁸ would only potentially apply to about 40% of breast cancer cases, which leaves much to discover to identify the causes for breast cancer.

An important avenue of research is the control of gene expression, since cancer is a disease characterized by abnormal transcription profiles, and an increasing number of studies reveal the impact of diet on the epigenome by chromatin-based mechanisms of gene expression control (referred to as epigenetic mechanisms).¹³ Breast cancer studies have pioneered the use of gene expression profiles to complement traditional methods for the subclassification of cancers at the molecular level and to link such subclasses to prognosis.¹⁹ The genome and associated epigenetic mechanisms have also been proposed to be one of the keys to understanding cancer development in response to environmental factors.^{20, 21; 22} Indeed, if the epigenome were shaped both via inheritance and the socioeconomical and cultural context, as the literature appears to indicate, each person or group of individuals might respond differently to environmental factors that modify disease risk. As an example, this concept of socioeconomical and cultural influence on epigenetic mechanisms might help explain why although low fat diets have been associated with a lower risk of developing breast cancer,²³⁻²⁴ effectiveness was not demonstrated in the large Women's Health Initiative trial.²⁵ To effectively develop primary prevention research, we need technologies that better assess the impact of disease risks on the epigenome of individuals, and that permit early evaluation of the efficacy of prevention strategies.

It has been only a few years following international recommendations such as the WCRF-AICR report,²⁶ since health authorities in many countries have begun the first campaigns on primary prevention to influence the population to adopt a healthy diet, mainly by eating fruits and vegetable in sufficient quantity. Primary prevention of chronic diseases is a new frontier in healthcare, which necessitates that we build a model of integrated methods to conduct research on risk at the population level, the cell biology level, the technology level and the social science level. Accounting for global diversity in nutrition and genome profiles offers great potential for determining effective diet interventions. In this article we first present a timely initiative- the International Breast Cancer and Nutrition (IBCN) collaboration- to illustrate the need for approaching research problems in chronic diseases in global teams and for building a primary prevention research infrastructure. Next, we give examples of how international interactions focused on breast cancer prevention are bringing momentum in primary prevention research that involves nutrition, and we discuss specific challenges of nutrition research in this endeavor.

Rationale behind the International Breast Cancer and Nutrition (IBCN) Collaboration

The IBCN collaboration was initiated in response to the rise of breast cancer incidence globally.^{9; 27} The range in variation in age-standardized breast cancer incidence is large, from as low as 8/100,000 to as high as 110/100,000.²⁷ Of particular concern are the rapid rise of incidence in LMI countries and the presence of aggressive forms of the disease in young women.^{28; 29; 30}

An urgent and complex situation

One of the difficulties in dealing with breast cancer is the diversity in types of neoplasias as shown by pathological classification as well as heterogeneity in gene expression profiles. Intriguingly, the possibility that a specific type of cancer might be determined early on (i.e., at the time of cancer onset) suggests that factors that control breast cancer risk themselves participate in the disease phenotype.^{20;13} Gene expression is controlled by the genetic and epigenetic heritage and by the environment that we consider broadly here to include impact from diet, exposure to chemicals and energy sources, lifestyle, and social groups. Among these factors diet is by far the most studied, and an increasing number of dietary factors are shown to influence epigenetic mechanisms. Indeed, dietary compounds that influence breast cancer development like folate, genistein (found in soy beans), tea polyphenols and resveratrol (found in red wine) can all affect central epigenetic mechanisms such as DNA methylation and histone modifications.¹³ Hence the relationship among nutrients, epigenome and breast cancer type is one of the complex interactions to solve. Furthermore, thorough analysis of the literature reveals that diet in early stages of life influences breast cancer risk.^{31; 32; 33; 34} This observation brings a sense of urgency in understanding how the risk level can be modified to prevent breast cancer onset in future generations.

It is troubling that many LMI countries cannot usually be included in the body of research on breast cancer risk factors. This is often due to the lack of preliminary data but also to the lack of studies developed as partnerships between high income and LMI countries. Moreover, analyses of population data to address the relationship between diet and breast cancer rarely explore the biological mechanisms of breast cancer initiation. Yet, nutrigenomics, the interaction of genes and diet, is a growing field due to recurrent demonstrations that dietary factors impact the expression of genes.^{35; 36; 37;13} Compelling evidence that diet can impact cancer incidence through generations has strengthened the hypothesis that the epigenetic inheritance might play a critical role in propagating the level of risk to develop such disease.

Challenges and priorities of primary prevention of breast cancer

The link between breast cancer and the environment may largely relate to the impact of diet on the epigenome of the breast epithelium before tumor development. Large scale genomic and transcriptomic analyses have been performed and epigenetic analyses are envisioned; however, they mainly use tumor tissues, hence rendering the identification of epigenetic modifications responsible for tumor onset difficult. The breast glandular system keeps remodeling via cell division throughout life, with developmental peaks *in utero*, at puberty and during pregnancy. These represent stages during which epigenetic modifications leading to increased risk of tumorigenesis could be propagated to the entire epithelial system or portions of the mammary gland. It will be particularly important to be able to recognize when, during the life span, the epigenetic effect of dietary compounds might be significant.

A major impairment in the development of primary prevention strategies for breast cancer is the paucity of markers of precursor signs of the disease. Currently the most effective way to evaluate a preventive action, including dietary intervention, is to wait several years and often almost a generation to see whether a tumor will develop.³⁸ Thus, the absence of knowledge regarding the factors contributing to breast cancer initiation and the lack of detection tools and validation of biomarkers of disease for early alterations that precede breast cancer development are important aspects on which we should focus. There might be some promising “omics” possibilities to catch breast cancer early based on epigenomics and metabolomics^{39; 40} and to detect a recurrence earlier than with mammography.⁴¹ For example, an increase in epigenetics-related polycomb protein EZ2H was observed 12 years before breast cancer development,⁴² which suggests that there might be opportunities to use epigenetics to monitor precursor changes related to neoplasia in the breast epithelium. Yet, the usefulness of earlier detection of a neoplastic process will be limited if no real preventive actions are available. Therefore, one of the immediate questions to answer is whether molecular markers of breast cancer risk, once established, could be used to assess a protective effect from a treatment or intervention.

The infrastructure to carry out global research is underdeveloped. Problems as complex as understanding diet and genetic/epigenetic interactions on prevalence of chronic disease, developing effective interventions to diminish disease risk, and translating the findings to populations of diverse cultures require a paradigm shift from current practice and training. By-laws and protocols for global teams to work together have to be developed and shared. Funding mechanisms for global work that span LMI and developed countries ought to be available. Strategies for developing public health messages that are effective, with global health impact are needed. We are attempting to coordinate such an effort for breast cancer prevention with the development of the International Breast Cancer & Nutrition (IBCN) collaboration.

Creation of a forum for primary prevention of breast cancer

The IBCN collaboration is a model for primary prevention. It was initiated by a group of scientists from life science and social science disciplines (www.purdue/IBCN) with the goal of promoting coordinated, yet country-tailored, interdisciplinary breast cancer prevention research and training world-wide. Understanding the relationship and mechanisms of interaction between diet and other lifestyle parameters, the epigenome, and the development of chronic diseases, in this case breast cancer, will bring an unprecedented insight into mechanisms that could be the source for prevention strategies (Figure 1). Four main objectives have been identified, (i) to develop an umbrella that favors cross-continental collaborations on any topic related to primary prevention of breast cancer; (ii) to organize a global project to decipher the link between diet, the epigenome and breast cancer types (Figure 1); (iii) to build a framework for international research via a good understanding of

societal and policy issues linked to primary prevention of breast cancer; and (iv) to encourage training in multidisciplinary, global research (see Table 1 for IBCN mission and goals). Communication with stakeholders in clinical and public health areas is a critical aspect of the project since primary prevention of noncommunicable diseases requires not only a different approach in research but also a change in mindset when considering healthcare. An international symposium appeared like a perfect forum to give momentum to this initiative.

Kick Off Symposium

The IBCN project was officially launched with an international symposium on breast cancer prevention held in October 2010 at Purdue University (www.purdue.edu/breastcancer). Scientists from different continents shared what is known about diet and breast cancer, how breast cancer is monitored and perceived in various countries, and how public health messages are best communicated.

The speakers reflected rich diversity in cultural beliefs and practices surrounding breast cancer. "There are 12 million cancer deaths annually; possibly 30% of them could be prevented", said Joe Harford, Director of the Office of International Affairs, National Cancer Institute. Primary prevention is the only way to reduce incidence. Yet we need strategies other than those currently focusing on decreasing risks that only account for cancer promotion in a small percentage of cases. We also need to tailor prevention initiatives for defined countries. For instance, Phillipe Autier, from the International Prevention Center in Lyon, France, argued that favoring breast-feeding would only have a marginal effect on decreasing breast cancer incidence among French women. Barriers to population awareness pertain to each country; they are grounded in culture and traditions. For example, in Ghana, breast cancer is often perceived as incurable so motivation to consult medical professionals is low. In Japan, the risk factors identified by the public are different from those identified by health professionals. In Canada, public health messages are not relevant to local populations that encompass different ethnic groups. Lack of cognizance of the cancer situation associated with a difficult economic context has delayed the development of cancer care plans in many countries. Consequently, there has to be a will for such a plan in order to even consider primary prevention initiatives.

Communicating prevention messages around the world is even more complex with the various channels that might have to be used based on culture for receiving communication in addition to different degrees of literacy levels. Messages are best targeted to lowering risk of early exposures to risk factors in puberty or earlier according to Kami Silk, Breast Cancer and Environment Research Center, Michigan State University.

Overall, nutritional effects on incidence of breast cancer are not well understood. "Many inconsistencies are evident", according to John Milner, then Chief of Nutritional Sciences Research Group, National Cancer Institute. Feeding practices which affect length of exposure to estrogen or which inhibit mammary cell proliferation, possibly by silencing genes that activate epidermal growth factor receptor⁴³ or affect transcription regulators like BRCA1 controlled by the estrogen receptor,⁴⁴ seem to be the most related to incidence of breast cancer. Dietary estrogenic constituents including phytoestrogens such as daidzein or genistein from soy foods or equol production from daidzein metabolized by gut microflora may influence vulnerability to breast cancer.⁴⁵ Moreover, diet changes that modify onset of menarche or menopause or induce amenorrhea may modify incidence of breast cancer. Some examples that support this hypothesis include the lower incidence of breast cancer with increasing number of children, at least 24 months combined breast-feeding, late menarche, early menopause, and higher BMI.²⁶ Weight gain before menopause, but retained

after menopause, is positively associated with breast cancer development.⁴⁶ Interestingly, weight reduction influences genomic imprinting.⁴⁷

Continuing with yearly symposia

The second symposium was held in Rennes, France from October 9 to 11, 2011. Holding symposia in different regions of the world not only embraces the spirit of global research, but it also sensitizes the region to primary prevention research and allows different countries to showcase their research initiatives in the field. The 2011 international breast cancer prevention symposium on “epigenetics, nutrition, and public policy” was organized as a partnership between Purdue University and the French School of Public Health (Ecole des Hautes Etudes en Santé Publique- EHESP). The central theme was epigenetics with impact on breast homeostasis and cancer development, the means to assess epigenetic modifications, the ethics surrounding the study of the genome and how it will impact the study of the epigenome, and the effect of diet on the epigenome. This symposium brought more participation from clinicians to add to the life scientists and social scientists (Figure 2A). Importantly, the international participation was greatly increased with 60% of people from outside Europe compared to 20% from outside North America in 2010, and 23 countries representing all regions of the world compared to 13 countries in 2010 (Figure 2B).

The speakers introduced the audience to the bases of epigenetics, how the environment may impact the epigenome, and how to study diet-epigenetic interactions. There are no examples of any diet exposure causing human disease through altering the epigenome to date⁴⁸. Furthermore, of the cancers, colorectal cancer may be more influenced by diet than breast cancer. “Structural abnormalities in cells are the carcinogens” according to Mina Bissell of the Lawrence Berkeley National Laboratory. For chromatin, cancer-related abnormalities are epigenetic and include global DNA hypomethylation, leading to genomic instability, and DNA hypermethylation of tumor suppressor gene promoters, leading to silencing of tumor suppression function⁴⁹; DNA methylation is naturally influenced by diet as certain nutrients are source of methyl groups. But whether to measure global DNA methylation, the alteration of which is a well-known effect of environmental exposures, or histone modifications because of their stability to uncover biomarkers of breast cancer risk, was a main point of debate at the symposium.

The influence of diet on any disease is most likely to have a determining effect in early life when the organism is undergoing developmental change as with fetal programming. Thus, the main impact of diet may be on succeeding generations.⁵⁰ There are three types of studies of diet and epigenetics according to Sharon Ross, National Cancer Institute, i.e. epidemiological or randomized controlled trials in humans, animal studies such as *in utero* exposures, and cell culture studies (for proof of principle). One example was a human study on the relationship of alcohol and folate intake on DNA methylation profiles in breast cancers.⁵¹ An example of a randomized trial was of two doses of soy isoflavones on methylation of cancer genes showing a dose response change in methylation reflecting levels of genistein.⁵²

Novel technologies allow dynamic epigenetic modifications of the nucleosome to be determined in single cells, which will require new developments in bioinformatics according to Joseph Irudayuraj and Rebecca Doerge of Purdue University. The ability to measure epigenetic modifications in single cells will allow variance in response to an intervention to be determined. On other aspects of the human genome, genotyping is currently useful to help guide difficult decisions for preventive surgery or treatment until better solutions encompassing all types of risks are developed. Joao Breda, WHO European Regional Office in Denmark, expects 10 new BRCA mutations to be identified through next generation

sequencing to further reflect options for those at risk of breast cancer. However, in order to develop effective prevention strategies, an important aspect of the research will be to understand how the type of mutations determines the level of breast cancer risk.

The ethics panel suggested that proactive steps for the ever increasing concern on confidentiality related to information on genes in individuals are prudent initiatives along with discovery research. One idea was to set up certificates of confidentiality on epigenomics.

In light of the discussions that took place during the three symposia organized by IBCN so far, with the latest symposium in 2012 focused on models for primary prevention, it was agreed that a better understanding of how diet may prevent or correct damage in the breast tissue can lead to primary prevention successes. An urgent research matter is to unravel how diet changes influence breast tissue homeostasis and gene expression.

Challenges to Global Research Projects on Nutrition

Answering the large research challenge of identifying the link between diet, epigenome and breast cancer will require modifying investigational approaches to diet and building a research and training infrastructure to support integration of multicultural nutritional information.

The many aspects of diet to take into account

The type of project described for IBCN poses the same issues recognized by nutrition epidemiologists for decades. Differences in many variables may confound apparent associations of diet. Although we may find dietary patterns or presence of bioactives that may be linked to a higher prevalence of breast cancer, there may be associated factors such as physical activity or exposure to carcinogens that may be the causal factors or that may interact with dietary factors to contribute to cancer onset. Thus, associational studies must be followed by other types of studies including animal studies to demonstrate causality.

Nutrition patterns change over time as convenience foods become available and are adopted by younger generations.⁵³ As a result, any geographical region may have a mix of diet comprised of foods from traditional and adopted cultures. It will be important to identify, whenever possible in each country, populations that have kept their diet clear from outside impact.

Interestingly, the impact of diet, even if it has modified the risk early in life, might be lasting because of an epigenetic action. Exposure to famine early in life led to imprinting on IGF-2 methylation 60 years later.⁵⁴ For instance, several dietary compounds have been shown to alter the epigenetic profile of tumor suppressor genes and oncogenes.¹³ Notably, the IGF-1 gene that produces a protein that favors breast cell proliferation is silenced through DNA methylation upon consumption of soy isoflavones.⁵² This particular type of epigenetic change can lead to sustained modifications in the expression of genes,^{55–56} then conveying breast cancer risk (or protection against cancer) through generations of cells in the breast, and possibly generations of individuals. Transmission of breast cancer risk to the offspring upon diet modification was elegantly demonstrated in animal studies. For instance, high fat diet fed to female rats during pregnancy was associated with shorter latency of induced mammary tumors in the offspring.⁵⁷ In light of the plethora of possible epigenetic modifications⁵⁸ it will be essential to classify the impact of nutrients based on their interaction with epigenetic mechanisms leading to either sustained or temporary effects. In particular, nutrients that have an impact on epigenetic mechanisms to temporarily affect gene expression (e.g., as long as the epigenetic modulator, like a particular nutrient, is

present) should not be disregarded. Indeed, even if of a nonpermanent type, this additional modification on an already fragile epigenome, because of sustained modifications suffered earlier in life, might be the trigger to cancer onset. Conversely, the presence of this particular nutrient and its nonpermanent epigenetic impact might prevent a permanent epigenetic risk from leading to cancer onset.

Financial and logistic support

Funding mechanisms are not in existence for global studies of diet and chronic disease. Support for research dealing with cancer, specifically breast cancer, has been strong, even increasing in a number of areas in high income countries. Nutrition research related to cancer has some targeted financial support in the USA. The question is whether funding agencies are prepared to support global studies on diet and cancer based on international work necessary to study the diversity of foods and epigenomes.

An additional challenge is the lack of funding for primary prevention research. There has been enhanced interest in primary prevention of cancers, but funding lags markedly behind that for research related to cures.⁵⁹ Yet economists agree that primary prevention of chronic diseases is more cost effective than disease treatment.⁶⁰ Therefore, support of primary prevention research globally should be a priority to help LMI countries win the fight against cancer. Many of these countries have other life-threatening concerns or an overall budget that will prevent them from bearing the costs of breast cancer detection technologies and treatments. A global project requires that any participating country be able to produce the collaborative work. Many LMI countries will not have funds to spare for this effort, and financial support will have to be made available from the broader international community, perhaps through specific bidirectional exchange programs. To convince policy-makers and funding agencies to bring substantial support in primary prevention research, an important project for economists interested in primary prevention of chronic diseases will be to calculate the public value of primary prevention research and interventions, notably those based on diet.

Gathering better funding for primary prevention research requires defining the models and tools to best perform primary prevention research. Models for primary prevention research were the focus of the third International Breast Cancer Prevention Symposium held at Purdue University (USA) in October 2012 (www.purdue.edu/breastcancer). The assumption has been that models that represent an existing disease also work as prevention models. This is true for secondary and tertiary prevention. However, for primary prevention, models will have to be developed and validated that represent stages occurring before a disease can be clinically diagnosed. There are still few models that appropriately mimic the various stages of breast cancer and even fewer models of initiation stages of the disease. Three-dimensional tissue culture systems⁶¹ and animal models⁶² of cancer initiation have already shown their great utility, but these models have to be perfected for the study of different breast cancer risk levels. Indeed, if diet influences the genome, the resulting effect of a particular diet will depend on the population, and even the individual with its own level of breast cancer risk. Furthermore, developing detection of precursor signs of the disease and preventive strategies will require using methods for screening preventive agents⁶³ and access to abnormal cells⁶⁴ in a different manner (i.e., noninvasive and nontoxic) compared to what has been done for cancer detection and treatment.

For successful international work, much effort is required to set up an effective infrastructure. One way to achieve such an organizational structure is to provide an adaptive framework with all partners involved and to subdivide the goals into tasks. The IBCN has developed a number of committees that are populated by scientists, clinicians and public health experts from all partner countries (Figure 3). This internal organizational structure is

complemented by an external Advisory Committee, an external Ethics Committee, and partnerships with international public health agencies including the International Agency for Research on Cancer (IARC) and the W.H.O. The external Advisory Committee reviews programs yearly against goals and objectives. The external Ethics Committee establishes guidelines for transcontinental work with human subjects. Interactions with international agencies provide contacts in countries of interest, information on the status of breast cancer in various regions of the world, and an understanding of the approach used to develop breast cancer-related prevention activities in different countries.

Early accomplishments of IBCN

Initiatives towards the achievement of goals set for IBCN, include development of the infrastructure to foster interdisciplinary collaborative research, design of novel technologies to study breast cancer risk and the student exchange program for cross-disciplinary training in primary prevention research.

Infrastructure to support research efforts

Two major committees constitute the engine for IBCN (Figure 3; www.purdue.edu/IBCN). The core committee is housed at Purdue University, the initiating institution of the global effort. It is comprised of faculty and administrators from a breadth of disciplines (basic medical sciences, statistics, nutrition, communication, healthcare, anthropology, health and kinesiology, engagement, engineering). This committee has established by-laws related to the functioning of IBCN committees and the participation of IBCN members that should facilitate global collaboration. It is the committee that provides sustainability in the interactions by initiating the organization of the annual IBCN symposium for the public and the affiliated strategic think-tank retreats for the IBCN teams. The committee provides a framework to accomplish the tasks identified during the strategic think-tank retreats. The second leading committee is the Executive Committee currently composed of members from each of the inaugural countries that launched the collaboration (France, Ghana, Uruguay, Lebanon, USA). Members of this committee coordinate collaborative efforts on primary prevention research for breast cancer for their own countries as well as with other countries from their region. These two committees have developed a 5-year strategic plan that is reviewed for progress assessment at the annual retreats.

The public relation/advertisement committee oversees the IBCN and symposium websites, and coordinates news regarding research efforts and activities related to primary prevention for immediate release throughout world regions in partnership with professional news media in partner countries. The data sharing committee provides all countries, regardless of their resources, a platform to compile and organize their data related to breast cancer as well as work with shared data. This committee is comprised of experts in database design that built our large scale collaborative HUB database.

The education and training committee fosters efforts to inform the public about primary prevention and epigenetics and facilitates the development of new courses focused on primary prevention research. An important aspect of the courses is to enable distance learning. A first course on mechanisms of international primary prevention research that includes a large portion on nutrition and breast cancer is offered at Purdue University and will become available for distance learning in early 2014.

Interdisciplinary collaborative projects

The strength in bioengineering at Purdue University has been a pillar for the initiation of collaborative research between physicists, biologists and nutritionists that has led to the development of a label-free Raman microspectroscopy method. Measurements based on

lipid orders in cell membranes in live tissue structures⁶³ are used to identify a change in the epithelial architecture (specifically apical polarity), recognized as an indicator of breast cancer risk.^{65,20,66} This technique will be used to screen for nutrients and their combinations that protect or endanger the breast epithelium. A pilot study demonstrated that $\omega 6$ -fatty acids rapidly altered tissue polarity. A project was also initiated to analyze the changes in epigenetic marks at single gene level on a per cell basis using fluorescence lifetime microscopy.⁶⁷ This capability is particularly important for breast cancer prevention research because of the increasing evidence that different types of breast cancers originate from different cell niches.⁶⁸ Some of the epigenetic markers to be investigated with this technology have been identified in a first approach by analyzing the effects of unrelated nutrients, i.e. fatty acids and folic acid, on epigenetic pathways in relation to the status of polarity in cell culture. Finally, collaboration among biologists and engineers led to the first breast-on-a-chip model that mimics the organization of the branched breast ductal system.⁶⁴ This model will be used for work linked to nutrigenomics within the breast tissue context as well as for the development of superparamagnetic nanotools for detection and treatment of abnormal breast epithelial cells following intraductal delivery, thus avoiding invasive therapeutic procedures.

A database on the epigenetic regulation of genes involved in breast cancer and cross-interaction with a nutrigenomic database focused on nutrients that have an epigenetic impact is currently under development (<http://ceehub.org/>). This project makes use of the web-based HUBzero technology developed at Purdue University^{69,70} and is founded on the analysis of the literature in nutrition, breast cancer, and the epigenome that was led by US and French IBCN scientists.¹³ The aim is to provide an unprecedented resource for the public and scientists to learn about the link between epigenetic profiles, breast genes, and the environment. This database will be useful to policy makers as well as to provide scientists with analyzable information for developing research hypotheses and for training in gene-nutrient interactions.

The sustainability of nascent international collaborative efforts like IBCN will occur through exchanges of students and faculty among partner countries. Already, IBCN graduate students have benefited from research awards funded through local fundraising efforts led by the PR/advertisement committee that supports the travel and living expenses of the students to partner institutions worldwide. One graduate student from a LMI country was awarded one of the 15 UNESCO-L'OREAL fellowships for women in science in 2012 for an exchange between the American University of Beirut and Purdue University for cross-training in biology, engineering and nutrition research, with a first publication recently profiled in a scientific web-community focusing on the mammary gland.⁷¹

Conclusion

Noncommunicable diseases (a category to which most forms of cancer belong) continue to receive far less attention than communicable diseases globally. Only obesity, considered an epidemic, is being recognized as a priority for primary prevention. Obesity indirectly influences cancer incidence but there is still much to explore when it comes to environmental effects on breast cancer prevention. The 2011 United Nations Summit on Noncommunicable diseases resulted in a call for governments, the private sector and the public society to develop plans by 2013 to act on risk factors for four major types of diseases, including cancers. Targeting the environment is among priority interventions to reduce disease risk, which is likely to have an impact on food and related public policy.⁷²

Diet and food are prime environmental factors that are modifiable, and therefore, amenable for public health messaging resulting from understanding their relationship to primary

prevention. Our global approach to deciphering the links between nutrition, epigenome and breast cancer has strengths anchored in the diversity of diet and epigenetic backgrounds that may alter the responsiveness to diet and in the possibility of tailoring interventions for individualized prevention. While the IBCN project is built around nutrition, this framework can be adapted to the study of other aspects of the environment (e.g., stress, exercise, pollutants) complementary to nutrition and to prevention of diseases other than breast cancer.

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REFERENCES

1. Food and Agriculture Organization Human vitamin and mineral requirements. Report of a joint FAO/WHO expert consultation. Bangkok, Thailand: World Health Organization, Rome; 2002.
2. Burlingame B, Nishida C, Uauy R, Weisell R. Joint FAO/WHO expert consultation: Fats and fatty acids in human nutrition. *Annals of Nutrition & Metabolism*. 2009; 55:1–308. [PubMed: 20104000]
3. Gonzalez CA. The European Prospective Investigation into Cancer and Nutrition (EPIC). *Public Health Nutr*. 2006; 9:124–126. [PubMed: 16512959]
4. Ziegler RG, Hoover RN, Pike MC, et al. Migration Patterns and Breast-Cancer Risk in Asian-American Women. *Journal of the National Cancer Institute*. 1993; 85:1819–1827. [PubMed: 8230262]
5. Maskarinec G, Noh JJ. The effect of migration on cancer incidence among Japanese in Hawaii. *Ethnicity & Disease*. 2004; 14:431–439. [PubMed: 15328946]
6. Ivers LC, Cullen KA, Freedberg KA, Block S, Coates J, Webb P. HIV/AIDS, Undernutrition, and Food Insecurity. *Clinical Infectious Diseases*. 2009; 49:1096–1102. [PubMed: 19725790]
7. Ronsmans C, Fisher DJ, Osmond C, Margetts BM, Fall CHD. Multiple micronutrient supplementation during pregnancy in low-income countries: A meta-analysis of effects on stillbirths and on early and late neonatal mortality. *Food and Nutrition Bulletin*. 2009; 30:S547–S555. [PubMed: 20120796]
8. Faruque AS, Ahmed AM, Ahmed T, et al. Nutrition: basis for healthy children and mothers in Bangladesh. *J Health Popul Nutr*. 2008; 26:325–339. [PubMed: 18831228]

9. World Cancer Report. Edited by Stuart, BW & Kleihues. International Agency for Research on Cancer. 2003
10. Boyle, P.; Levin, B., editors. World Cancer Report. International Agency for research on Cancer. 2008.
11. Key TJ, Allen NE, Spencer EA, Travis RC. The effect of diet on risk of cancer. *Lancet*. 2002; 360:861–868. [PubMed: 12243933]
12. Globocan. [accessed 2/11/2013] 2008. <http://globocan.iarc.fr/factsheet.asp>
13. Teegarden D, Romieu I, Lelievre SA. Redefining the impact of nutrition on breast cancer incidence: is epigenetics involved? *Nutr Res Rev*. 2012; 25:68–95. [PubMed: 22853843]
14. Michels KB, Mohllajee AP, Roset-Bahmanyar E, Beehler GP, Moysich KB. Diet and breast cancer a review of the prospective observational studies. *Cancer*. 2007; 109:2712–2749. [PubMed: 17503428]
15. Sonestedt E, Gullberg B, Wirfalt E. Both food habit change in the past and obesity status may influence the association between dietary factors and postmenopausal breast cancer. *Public Health Nutr*. 2007; 10:769–779. [PubMed: 17381916]
16. Park S, Bae J, Nam BH, Yoo KY. Aetiology of Cancer in Asia. *Asian Pacific Journal of Cancer Prevention*. 2008; 9:371–380. [PubMed: 18990005]
17. Day GE, Lanier AP, Bulkow L, Kelly JJ, Murphy N. Cancers of the Breast, Uterus, Ovary and Cervix among Alaska Native Women, 1974–2003. *International Journal of Circumpolar Health*. 2010; 69:72–86. [PubMed: 20167158]
18. Parkin DM, Boyd L, Walker LC. 16. The fraction of cancer attributable to lifestyle and environmental factors in the UK in 2010. *Br J Cancer*. 2011; 105(Suppl 2):S77–S81. [PubMed: 22158327]
19. Wesolowski R, Ramaswamy B. Gene Expression Profiling Changing Face of Breast Cancer Classification and Management. *Gene Expression*. 2011; 15:105–115. [PubMed: 22268293]
20. Lelièvre SA. Tissue polarity-dependent control of mammary epithelial homeostasis cancer development an epigenetic perspective. *J Mammary Gland Biol Neoplasia*. 2010; 15:49–63. [PubMed: 20101444]
21. Pozharny Y, Lambertini L, Clunie G, Ferrara L, Lee MJ. Epigenetics in Women's Health Care. *Mount Sinai Journal of Medicine*. 2010; 77:225–235. [PubMed: 20309920]
22. Riscuta G, Dumitrescu RG. Nutrigenomics implications for breast and colon cancer prevention. *Methods Mol Biol*. 2012; 863:343–358. [PubMed: 22359305]
23. Brennan SF, Cantwell MM, Cardwell CR, Velentzis LS, Woodside JV. Dietary patterns breast cancer risk a systematic review and meta-analysis. *Am J Clin Nutr*. 2010; 91:1294–1302. [PubMed: 20219961]
24. Ronco AL, De Stefani E, Stoll M. Hormonal and metabolic modulation through nutrition towards a primary prevention of breast cancer. *Breast*. 2010; 19:322–332. [PubMed: 20542695]
25. Prentice RL, Caan B, Chlebowski RT, et al. Low-fat dietary pattern risk of invasive breast cancer the Women's Health Initiative Randomized Controlled Dietary Modification Trial. *JAMA*. 2006; 295:629–642. [PubMed: 16467232]
26. World Cancer Research Fund and American Institute for Cancer Research. Food, nutrition, physical activity, and the prevention of cancer: a global perspective. Washington DC: 2007. p. 289–298.
27. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008 GLOBOCAN 2008. *Int J Cancer*. 2011; 127:2893–2917. [PubMed: 21351269]
28. Huo D, Ikpat F, Khramtsov A, et al. Population differences in breast cancer survey in indigenous African women reveals over-representation of triple-negative breast cancer. *J Clin Oncol*. 2009; 27:4515–4521. [PubMed: 19704069]
29. Freedman RA, Partridge AH. Adjuvant therapies for very young women with early stage breast cancer. *Breast*. 2011; 20(Suppl 3):S146–S149. [PubMed: 22015283]
30. André C, Collignon J, Rorive A, et al. Breast cancer in young women. *Rev Med Liege*. 2011; 66:397–399. [PubMed: 21826983]

31. Hilakivi-Clarke L, Andrade JE, Helferich W. Is Soy Consumption Good or Bad for the Breast? *Journal of Nutrition*. 2010; 140:2326s–2334s. [PubMed: 20980638]
32. Eskelinen M, Ollonen P. Life Stress due to Losses Deficit in Childhood Adolescence as Breast Cancer Risk Factor A Prospective Case-Control Study in Kuopio, Finland. *Anticancer Research*. 2010; 30:4303–4308. [PubMed: 21036756]
33. Sangaramoorthy M, Phipps AI, Horn-Ross PL, Koo J, John EM. Early-life factors breast cancer risk in Hispanic women the role of adolescent body size. *Cancer Epidemiol Biomarkers Prev*. 2011; 20:2572–2582. [PubMed: 22056503]
34. Pearce MS, Tennant PW, Mann KD, et al. Lifecourse predictors of mammographic density the Newcastle Thousand Families cohort Study. *Breast Cancer Res Treat*. 2011; 131:187–195. [PubMed: 21833624]
35. Burdge GC, Lillycrop KA. Bridging the gap between epigenetics research and nutritional public health interventions. *Genome medicine*. 2010; 2:80. [PubMed: 21067534]
36. McKay JA, Mathers JC. Diet induced epigenetic changes and their implications for health. *Acta Physiologica*. 2011; 202:103–118. [PubMed: 21401888]
37. Parasramka MA, Ho E, Williams DE, Dashwood RH. MicroRNAs, diet, and cancer: New mechanistic insights on the epigenetic actions of phytochemicals. *Molecular Carcinogenesis*. 2012; 51:213–230. [PubMed: 21739482]
38. Martin LJ, Li Q, Melnichouk O, et al. A randomized trial of dietary intervention for breast cancer prevention. *Cancer Res*. 2011; 71:123–133. [PubMed: 21199800]
39. Slupsky CM, Steed H, Wells TH, et al. Urine metabolite analysis offers potential early diagnosis of ovarian and breast cancers. *Clin Cancer Res*. 2010; 16:5835–5841. [PubMed: 20956617]
40. Sugimoto M, Wong DT, Hirayama A, Soga T, Tomita M. Capillary electrophoresis mass spectrometry-based saliva metabolomics identified oral, breast and pancreatic cancer-specific profiles. *Metabolomics*. 2010; 6:78–95. [PubMed: 20300169]
41. Asiago VM, Alvarado LZ, Shanaiah N, et al. Early detection of recurrent breast cancer using metabolite profiling. *Cancer Res*. 2010; 70:8309–8318. [PubMed: 20959483]
42. Ding L, Erdmann C, Chinnaiyan AM, Merajver SD, Kleer CG. Identification of EZH2 as a molecular marker for a precancerous state in morphologically normal breast tissues. *Cancer research*. 2006; 66:4095–4099. [PubMed: 16618729]
43. Sakla MS, Shenouda NS, Ansell PJ, Macdonald RS, Lubahn DB. Genistein affects HER2 protein concentration, activation, and promoter regulation in BT-474 human breast cancer cells. *Endocrine*. 2007; 32:69–78. [PubMed: 17992604]
44. Fan S, Meng Q, Auburn K, Carter T, Rosen EM. BRCA1 and BRCA2 as molecular targets for phytochemicals indole-3-carbinol and genistein in breast and prostate cancer cells. *Br J Cancer*. 2006; 94:407–426. [PubMed: 16434996]
45. NAMS. Isoflavones report: The role of soy isoflavones in menopausal health: report of The North American Menopause Society/Wulf H. Utian Translational Science Symposium in Chicago, IL (October 2010) *Menopause*. 2011. p. 732-753. <<http://www.ncbi.nlm.nih.gov/pubmed/21685820>>. Edited by Chicago
46. Vrieling A, Buck K, Kaaks R, Chang-Claude J. Adult weight gain in relation to breast cancer risk by estrogen progesterone receptor status a meta-analysis. *Breast Cancer Res Treat*. 2010; 123:641–649. [PubMed: 20711809]
47. Waterland RA, Jirtle RL. Early nutrition, epigenetic changes at transposons and imprinted genes, and enhanced susceptibility to adult chronic diseases. *Nutrition*. 2004; 20:63–68. [PubMed: 14698016]
48. Waterland, RA. Nutritional epigenetics. In: Erdman, JW.; McDonald, I.; Zeisel, S., editors. *Present Knowledge in Nutrition*. 10th ed.. Ames, Iowa: Wiley-Blackwell; 2012. p. 14-26.
49. Ehrlich M, Lacey M. DNA hypomethylation and hemimethylation in cancer. *Adv Exp Med Biol*. 2012; 754:31–56. [PubMed: 22956495]
50. Lundgren EM, Cnattingius S, Jonsson B, Tuvemo T. Intellectual and psychological performance in males born small for gestational age with and without catch-up growth. *Pediatr Res*. 2001; 50:91–96. [PubMed: 11420424]

51. Christensen BC, Kelsey KT, Zheng S, et al. Breast cancer DNA methylation profiles are associated with tumor size and alcohol and folate intake. *PLoS Genet.* 2011; 6:e1001043. [PubMed: 20686660]
52. Qin W, Zhu W, Shi H, et al. Soy isoflavones have an antiestrogenic effect and alter mammary promoter hypermethylation in healthy premenopausal women. *Nutr Cancer.* 2009; 61:238–244. [PubMed: 19235040]
53. Popkin BM, Adair LS, Ng SW. Global nutrition transition and the pandemic of obesity in developing countries. *Nutr Rev.* 2012; 70:3–21. [PubMed: 22221213]
54. Gluckman PD, Hanson MA, Bateson P, et al. Towards a new developmental synthesis adaptive developmental plasticity and human disease. *Lancet.* 2009; 373:1654–1657. [PubMed: 19427960]
55. Jousse C, Parry L, Lambert-Langlais S, et al. Perinatal undernutrition affects the methylation and expression of the leptin gene in adults implication for the understanding of metabolic syndrome. *FASEB J.* 2011; 25:3271–3278. [PubMed: 21670064]
56. Przybilla J, Galle J, Rohlf T. Is adult stem cell aging driven by conflicting modes of chromatin remodeling? *Bioessays.* 2012; 34:841–848. [PubMed: 22821708]
57. de Assis S, Khan G, Hilakivi-Clarke L. High birth weight increases mammary tumorigenesis in rats. *Int J Cancer.* 2006; 119:1537–1546. [PubMed: 16646052]
58. Waldmann T, Schneider R. Targeting histone modifications-epigenetics in cancer. *Curr Opin Cell Biol.* 2013 [Epub 2013/01/26].
59. National Cancer Institute: 2010. Fact Book. US Department of Health and Human Services; 2010.
60. Hillner BE, Smith TJ. Allocating cancer-directed expenditures tensions between prevention, early detection and treatment is unnecessary. *Recent Results Cancer Res.* 2011; 188:1–9. [PubMed: 21253785]
61. Vidi PA, Bissell MJ, Lelièvre SA. Three-dimensional culture of human breast epithelial cells the how and the why. *Methods Mol Biol.* 2013; 945:193–219. [PubMed: 23097109]
62. Sierra A. Animal models of breast cancer for the study of pathogenesis and therapeutic insights. *Clin Transl Oncol.* 2009; 11:721–727. [PubMed: 19917535]
63. Yue S, Cardenas-Mora JM, Chaboub LS, Lelièvre SA, Cheng JX. Label-free analysis of breast tissue polarity by Raman imaging of lipid phase. *Biophys J.* 2012; 102:1215–1223. [PubMed: 22404944]
64. Grafton MM, Wang L, Vidi PA, Leary J, Lelièvre SA. Breast on-a-chip mimicry of the channeling system of the breast for development of theranostics. *Integr Biol (Camb).* 2011; 3:451–459. [PubMed: 21234506]
65. Chandramouly G, Abad PC, Knowles DW, Lelièvre SA. The control of tissue architecture over nuclear organization is crucial for epithelial cell fate. *J Cell Sci.* 2007; 120:1596–1606. [PubMed: 17405811]
66. Maxwell CA, Benitez J, Gomez-Baldo L, et al. Interplay between BRCA1 and RHAMM regulates epithelial apicobasal polarization and may influence risk of breast cancer. *PLoS Biol.* 2011; 9:e1001199. [PubMed: 22110403]
67. Chen J, Miller A, Kirchmaier AL, Irudayaraj JM. Single-molecule tools elucidate H2A.Z nucleosome composition. *J Cell Sci.* 2012; 125:2954–2964. [PubMed: 22393239]
68. Molyneux G, Smalley MJ. The cell of origin of BRCA1 mutation-associated breast cancer a cautionary tale of gene expression profiling. *J Mammary Gland Biol Neoplasia.* 2011; 16:51–55. [PubMed: 21336547]
69. Qiao W, McLennan M, Kennell R, Ebert DS, Klimeck G. Hub-based simulation and graphics hardware accelerated visualization for nanotechnology applications. *IEEE Trans Vis Comput Graph.* 2006; 12:1061–1068. [PubMed: 17080835]
70. Melcher J, Hu S, Raman A. VEDA: a web-based virtual environment for dynamic atomic force microscopy. *Rev Sci Instrum.* 2008; 79:061301. [PubMed: 18601390]
71. Bazzoun D, Lelièvre S, Talhouk R. Polarity proteins as regulators of cell junction complexes: Implications for breast cancer. *Pharmacol Ther.* 2013 [Epub ahead of print, 2013 Feb 28].
72. Magnusson R, Patterson D. Role of law in global response to non-communicable diseases. *Lancet.* 2011; 378:859–860. [PubMed: 21890035]

Figure 1. Model for the IBCN research project

Part of the IBCN project will be common to all partner countries with the goal to understand the link between the epigenome, dietary habits and the development of specific types of breast cancer. This project will rely on strong bases from communication, technologies and population studies for its development. It will expand worldwide into translational work thanks to partnership with anthropologists, engineers and economists and experts in behavior. The outcomes of the project will encompass the design and testing of intervention strategies for primary prevention of breast cancer and the influence on public policy that will facilitate primary prevention efforts.

Figure 2. Outcomes from the first two international breast cancer prevention symposia
 The IBCN has developed multidisciplinary meetings to facilitate the creation of an international community focused on primary prevention of breast cancer. The 2010 symposium was held at Purdue University, West Lafayette, Indiana (USA), October 8–10, 2010 and the second symposium was held in Rennes (France), October 9–11, 2011. **A.** Bar graph of the percentage of participants based on different regions of the world. **B.** Percentage of participants per field. Admin = administrators from education and funding areas; advocates = consumer advocates and research advocates in the area of breast cancer; social science (sc) (education, communication, anthropology, policy, health law, economics); natural sc (biology, biochemistry, biophysics, biostatistics, computational science, nutrition, epidemiology).

International breast cancer and nutrition project- Organizational chart

Figure 3. Organizational chart of IBCN

All IBCN members of partner countries can participate in the executive committee that runs the project in partnership with the Purdue University-based Core Committee. With the exception of External Advisory and Ethics Committees, IBCN members also populate the other committees as defined in the project by-laws. Each committee had its own agenda defined in part during annual strategy think-tanks.

Table 1

Mission & Goals of the International breast cancer & nutrition (IBCN) collaboration as listed in the current strategic plan (October 2012)

MISSION

The mission of the IBCN project is to foster the development of a community of scientists across disciplines, public health experts and stakeholders dedicated to research on the primary prevention of breast cancer. Within this mission IBCN is also designing an international, multidisciplinary and integrated collaborative program to identify the impact of nutrition on breast cancer onset (and recurrence) and to elucidate the cellular and molecular mechanisms involved in nutrient-induced breast tissue alterations and cancer development. The anticipated outcomes of this program are the development of strategies to diminish breast cancer incidence and/or incidence of aggressive forms of breast cancer based on epidemiological and biological findings related to nutrition and an impact on public policies via information of the public and health authorities. Although the research efforts are focused on primary prevention to diminish the risk of developing breast cancer, any possibility that the discoveries might be applied to prevent breast cancer recurrence would also be pursued.

GOALS

- I. Identify the potential links among diet, epigenomic characteristics and breast cancers.
- II. Create new models for understanding the biological (i.e., intrinsic to the human organism) and environmental factors that contribute to breast cancer incidence.
- III. Design a primary prevention model that can be generalized to examine biological and environmental factors responsible for the incidence of other chronic diseases.
- IV. Identify targets and strategies to prevent breast cancer development.
- V. Translate discoveries to global communities.