Editorial

Challenges and opportunities of applying P4 medicine and traditional Chinese medicine for cancer treatment and prevention in the 21st century: A medical oncologist's perspectives

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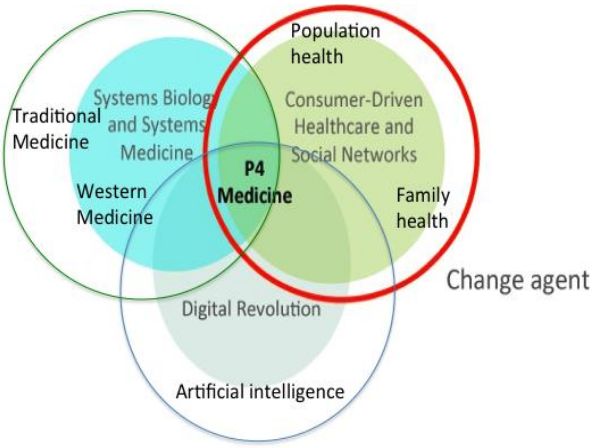
Highlights:
Being one of the deadliest diseases with ever-rising incidence especially in China, cancer is a major health threat and drains the patients, their families and society more resources than all other diseases. This overview on colorectal cancer treatment and prevention intends to rally principle-based P4 medicine (predictive, preventative, personalized and participatory) practice and best of traditional Chinese medicine on pre-illness and disease prevention and treatment to lead 21st century consumer driven health care and network movement facilitated by inevitable digital revolution and artificial intelligence use in every day's life.



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Challenges and opportunities of applying P4 medicine and traditional Chinese medicine for cancer treatment and prevention in the 21st century: A medical oncologist's perspectives

Edward H. Lin

Abstract: Being one of the deadliest diseases, cancer needs a stronger dose of P4 medicine (Predictive, Preventive, Personalized and Participatory) first proposed by Dr. Hood and TCM intervention, as cancer treatment still largely relies on the decade-old cytotoxic chemotherapy, radiation and surgery. This overview uses colorectal cancer model to discuss pitfalls in current cancer prevention and treatment strategies, which saw many randomized phase III studies failing to meet the study primary endpoints or marginally meeting the study objectives. Complete sequencing of whole human genome provided much of the hopes as well as hypes for precision medicine, as genomic diversity, ever changing tumor mutation landscape, SNP and complex microRNA regulation from the intron region and epigenetics make genotype to phenotype correlation study increasingly challenging. As a participant of One hundred Persons Pioneers Project, I witnessed first hand how a comprehensive scientific wellness study that integrates whole genomics, microbiome, and metabolome nutrition along with comprehensive laboratory examinations can be used to diagnose pre-illness in all "healthy" participants. Pre-illness can be best intervened by none pharmaceutical means and traditional Chinese Medicine (TCM) adept in restoring internal healing mechanisms, opening up the blocked network and balancing the five-elements homeostasis. Following TCM principles, we were able to design a therapy that effectively targets colon cancer stem cells and its microenvironment leading to more doubling of overall survival with reduction in overall toxicities. Pre-illness diagnosis, cancer immunotherapy, TCM medicine is about restoring internal healing power by letting go brakes on "good" immune systems to go after the "bad" cancer cells. Time is ripe to integrate our knowledge in genomics immune systems, stem cell biology, nutrition, inflammation, metabolism, systems medicine, and modern TCM to deliver a level of care that most of major illness including cancer are now minor pre-illness and are delayed, prevented, or cured at their earliest stages along with elevation in healthy index in the individual, their families and society as a whole globally.

Key words： P4 Medicine, Traditional Chinese medicine, Cancer treatment, Cancer prevention.

摘要

癌症作为最致命的疾病之一，其治疗在很大程度上仍然沿用着数十年前就出现的化疗、放疗、手术等方式，因此迫切需要更多地 P4 医学以及传统中医的干预，P4 医学由 Hood 博士最先提出，是一种预测性、预防性、个性化和参与性相结合的医学概念。鉴于许多随机 III 期临床研究无法满足其主要研究终点或者只能勉强达到研究目标，因此本综述利用结直肠癌模型来讨论当前癌症预防和治疗策略中存在的误区。人类全基因组测序的完成为精准医学带来了很大的希望，同时也带来了大量的宣传炒作。基因组多样性、不断变化的肿瘤突变形势、SNP、源于基因内含子区域的复杂 microRNA 调控、表观遗传学等这些因素，都使得基因型与表型的相关性研究变得越来越具挑战性。作为 100 先锋项目的一名参与者，我亲眼目睹了这个项目是如何为所谓"健康"的参与者诊断未病的过程。100 先锋项目是一个全面、科学的健康研究项目，该项目包含了全基因组学、微生群落学、营养学以及全面的实验室检查等研究手段。非药物疗法和传统中医能够对未病产生很好的干预效果，传统中医擅长于恢复人体内部的自愈机制、打开人体闭塞的经络以及平衡人体的五行。根据传统中医的原则规律，我们设计了一种疗法，这种疗法能够有效地对结肠癌干细胞及其所处的微环境产生靶向作用，使患者总生存期提高一倍多，并且降低总体药物的毒副作用。未病的诊断、癌症免疫疗法、传统中医都是通过对"好"的免疫系统放开限制，让其去追捕人体"坏"的癌细胞，从而恢复人体内部的自愈能力。是时候将基因组学、免疫学、干细胞生物学、营养学、炎症研究、代谢学、系统医学和现代中医学等知识融合在一起了。这样我们就能达到一个新的医疗护理水平，使得包括癌症在内的大部分重大疾病、以及轻微的未病在早期就能得到推迟、预防或治愈，同时在全球范围内实现个人、家庭和社会整体健康指数的提高。

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Introduction

For decades, three main pillars of cancer therapy are chemotherapy, radiation and surgery. Many of the cancer prevention and treatment researches were driven by six hallmarks of cancer elegantly summarized by Hanahan and Weinberg [1]. Cancer researchers quickly realized that targeting cancer cells were not adequate and had turned their attentions to cancer genomics, immune evasion and cancer microenvironment which were added as new cancer hallmarks that will drive next generation cancer prevention and treatment clinical trials [2]. Given the space limitations, we highlight achievements and pitfalls of the current colorectal cancer prevention and treatment strategies to argue for a new integrated principle-based P4 medicine and traditional Chinese medicine (TCM) guides driving next generation of global cancer prevention and treatment strategies.

5FU had been used to treat colorectal cancer for five decades. Only till recently did we witness FDA approvals of nine targeted agents for colorectal cancer treatment now endorsed by National Cancer Center Network guidelines and more of the new agents are coming [3]. However, none of these new agents has ever challenged supreme position of 5-FU, or fluoropyrimidine, which remain as the backbone agent for colorectal cancer treatment. Some of the new agents even have had difficulties in global marketing thanks to asymmetric global regulatory policy on staggering cost and most importantly, lack of clinically meaningful gain in overall survival [4-7]. Completion of whole human genome sequencing and cancer genome atlas provided much of the hopes as well as hypes for the so-called precision medicine initiatives and cancer moonshot program by major cancer centers in the US [8-10] and in China.

National Cancer Institute had to increase the power of the NCI Match Trial from 3,000 cancer patients to 5,000 cancer patients' trial in order to find mutations match through next generation sequencing (NGS) to the selected targeted drugs and so far about 9% of the mutations had resulted in matched drugs which may or may not lead to therapeutic benefits [11]. This industrial approach makes an assumption that mutation (s) are static driver mutations and targeting these mutation (s) could lead to therapeutic benefits. Such reductionist approaches overlook the importance of dynamic genes mutations and their networks of interactions possibilities that can affect efficacies as well as toxicities of such interventions.

To address the fact that no one genome or mutations can be equally randomized and ever-increasing cost of reactive care with limited survival gain, Dr. Lee Hood, a founding figure of immunology, biotechnology, and systems biology foresee the integration of sophisticated biological instrumentation, the human genome, systems biology; and digital and consumer health revolution to new frontier of medicine: P4 medicine which stands for Predictive, Preventive, Personalized and Participatory medicine, contrary to today's reactive guideline driven medical practices [12]. P4 medicine did not gain much traction since it was first pitched to the medical community eight years ago when the use genomic technology has yet to prove that it can change standard of care and save lives. P4 medicine promotes the integration of systems medicine technology (omics), digital revolution, and consumer directed health initiatives to drive health care need. With crowd source funding, Dr. Hood and his institute for Systems Biology launched 100 pioneer study two years ago utilizing fitbit to track sleep and physical activity, whole genome sequencing, inflammation, microbiome, and metabolome, nutrition along with routine medical examination along counseling support [13].

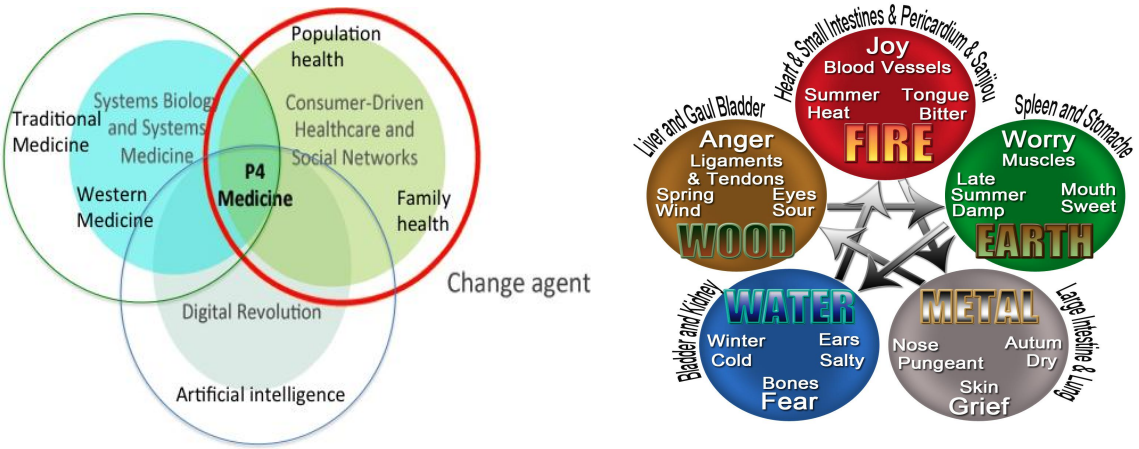

Figure 1. P4 medicine represents convergence of consumer driven health movement, Digital revolution that lead to ready access of information and systems medicine and TCM medicine as governed by five health elements which is linked to internal organs and psychosocial and emotional wellbeing.

As one of the research subjects (participatory), I was among a few physician volunteers who tasted first dose of P4 medicine diagnostics and interventions. Like all other "healthy" volunteers, we all harbor some form of subclinical imperfections in area of metabolism, nutrition, inflammation akin to "pre-illness" that traditional Chinese medicine (TCM) practitioners may be more adept in devising an integrated, least toxic and proven effective interventions including acupuncture, herbal remedies, and physical therapy beside application of large scale public health databases. In this review, we propose a principle based P4 medicine practice integrating best of eastern and western medicine in devising a new generation of personalized diagnostics, prevention and treatment protocols (Figure 1).

Ten Hallmarks of cancers and lessons from colorectal cancer treatment and preventions narrows to immune angle

Cancer researchers took almost a decade shifting from six hallmarks of cancer i.e. limitless cell proliferation; Invasion; evasion of death; immortality; metastasis; and tumor angiogenesis [1] to immune evasion, and tumor microenvironment [2] driven by the clinical success of applying the checkpoint inhibitors [14-17]. The level of enthusiasms for cancer immunotherapy was similar to the era when concept of targeting tumor angiogenesis was first reported [18]. In fact, the first phase I clinical trial evaluating endostatin, the first anti-angiogenic agent was met with such enthusiasm that thousands more cancer patients signed up only to find that they needed to go through a lottery system to enroll in this clinical trial. In the end, endostatin was abandoned altogether for development in the US. Anti-angiogenesis therapy in cancer led to a moderate two months gain in overall survival as compared to standard of care across all solid tumors and bevacizumab was first approved by the FDA which then voted later on to remove breast cancer from In the ensuing decades, researchers learned that these cancer cells are genomicallly unstable, and quickly evades various treatments through energy reprogramming as the tumors can survive in much harsher microenvironments to evade effects of chemotherapy, radiation and immune surveillance [2]. This positional cancer hallmark paper will have a profound impact for this generation of cancer researchers on their treatment and prevention strategies; For space reasons, we will limit this overview to colorectal cancer prevention and treatment only. Colorectal cancer carcinogenesis takes two to three decades to evolve from precancerous polyp through a series of mutations to invasive cancer. Long-term regular use of aspirin or NSAIDs significantly reduce CRC recurrence risks [21], so will vitamin D, exercise, and control of colon cancer risk factors (obesity, diabetes, smoking and alcohol) could reduce colorectal cancer risks [22, 23]. Unlike aspirin, several large-scale cancer prevention trials using singular nutritional intervention i.e. Vitamin E, selenium and calcium did not demonstrate the reduction of colon polyp or cancer incidence despites strong preclinical rationales. It is interesting that aspirin is derived from plant hormone salicylic acid, which governs wide range of cellular functions including immune response, thermogenesis, respiration, fruit yield, seed germination and DNA repair immune modulation with strong parallel to cell biology found in mammalian cells where aspirin, a synthetic acetyl salicylic acid have properties in mammalian cells and functions as antipyretic, anti-inflammatory, prevention of pre-cancer and cancer, anti-platelets aggregation, ovulation, thrombosis and prevention of cardiovascular events and stroke. There are toxicities related to aspirin i.e. GI ulcer and serious CNS bleeding which is dose related (Figure 2).

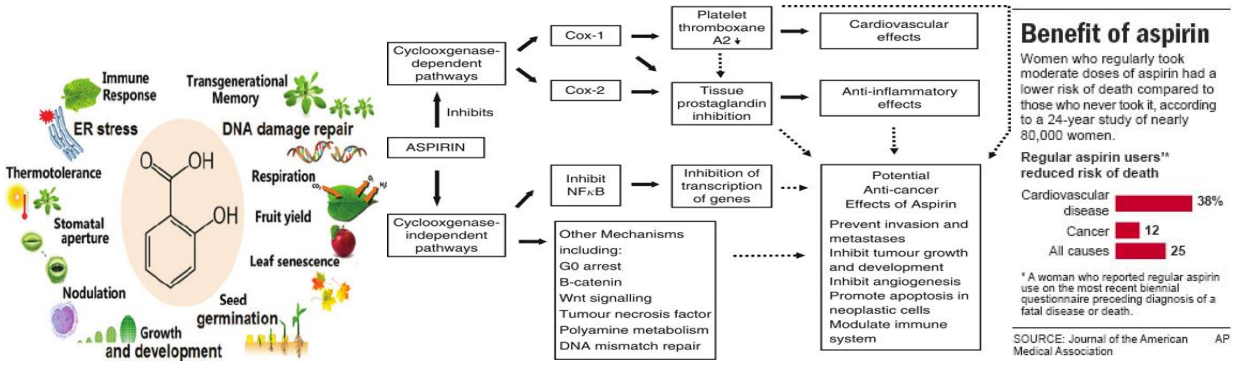

Figure 2. Versatile functions of plant hormone salicylic acid (a derivative to aspirin) in regulating plants' immune response, thermogenesis, respiration, fruit yield, seed germination and DNA repair. Striking parallel of these plant functions were found aspirin, acetyl salicylic acid which inhibits both COX-1 and COX-2 in mammalian cells and functions as antipyretic, anti-inflammatory, prevention of pre-cancer and cancer distant metastases, anti-platelets aggregation, ovulation, thrombosis and prevention of cardiovascular events and stroke. Side effects include GI ulcer, CNS bleeding diathesis, and renal injuries.

On the therapeutic front, FDA had approved nine agents for colorectal cancer, however, 5-FU or fluoropyrimidine still remain as the backbone of chemotherapy alone or in combination with other chemotherapy agents or radiation [3]. Most of these novel targeted agents are making incremental 1.4-2 months gain in median survival as compared to the control. As directed by the cancer hallmarks, there are three agents that target tumor DNA directly i.e. 5FU irinotecan and oxaliplatin, while rests bevacizumab and aflibercept, regorafenib are targeting vascular endothelial growth factor (VEGF) pathways, and panitumumab and cetuximab, are targeting epidermal growth factor receptor (EGFR) pathways [4-7]. While some of the agents e.g. bevacizumab or oxaliplatin do not have activities in the absence of 5FU, none of the agents were able to challenge the 5FU backbone. Interestingly, 5FU is largely ineffective against a small subset of colorectal cancers that harbor microsatellite instability (MSI-H). In contrast, a checkpoint inhibitor, pembrolizumab resulted in promising high rate of tumor responses in MSI-H colorectal cancers as the response correlate with their high mutation loads, which may in turn have elicited inherent anti-tumor immune responses [14]. Interestingly, the observed anti-tumor effects of aspirin in colorectal cancer polyp and cancer prevention is also stemming from its immune and inflammatory modulation through PD-1 and PGE2 respectively [24]. Likewise, 5-FU also has anti-cancer properties through its immune modulatory activities to be discussed in the later section.

Immune is the ultimate link to modern anti-cancer therapies and opportunities for TCM

Scientists from the reductionist camp also long recognized over simplifications of complex, intricately interconnected biological organism rather than a "one gene or one protein" function in a vacuum. For a complex disease like cancer, there are ever-evolving molecular mutations or targets beside some of the high profiles that have been successfully exploited for targeted therapy: CD20, [25] Her2/Neu, [26] Bcl-abl [27] c-kit [28] and Bruton tyrosine Kinase (BTK) [29]. Finding similar one-on-one molecular switches or targeting for high mutation load solid tumors would not be an easy feat. Clues from the ancient Chinese remedy book had yielded the FDA approval of arsenic trioxide as the main treatment of acute promyelocytic leukemia [30]. The part of the anti-tumor mechanisms with arsenic trioxide is related at least in part to the its immune toxicities in the immunosuppressive network and boost in innate immunity. More recently, checkpoint inhibitors yielded 20% durable responses in tumors that are otherwise unresponsive to the cytotoxic chemotherapy such as 5FU in colorectal cancer [14]. In fact, responses to checkpoint inhibitors correlate with the underlying high mutation load of the tumor. It is no surprise that only repertoires of T cells immunity can rival high mutation load of tumors. So far the toxicities with the use checkpoint point inhibitors have been very manageable but toxicities for combination immunotherapy began to mount especially in recent use of CAR-T [14-17]. In fact, chronic arsenic trioxide are toxic to immune systems and its anti-leukemic effects were through eliminate immune suppressive component will in turn boost of immune surveillance function through a complex molecular mechanism [31].

Therefore, future global cancer treatment and prevention efforts will need to examine best strategies to mobilize one's inactivated anti-cancer immune systems without suffering any major side effects. Immune systems and inflammation are double edge swords and harnessing their awesome healing power within for cancer treatment and prevention dealt a right card into the hands of TCM as it founding principle are all about homeostasis and five health element balance and activating one internal healing powers without major disruption of the host health ecosystems. TCM practitioners are now presented with unprecedented opportunities to work with forward thinking reductionist trained physicians, cancer immunologists and specialists, and system biologist and scientists to form a new research alliance to charter a new path of TCM principle based P4 system medicine practice, in charge of designing and implementing a series of highly personalized cancer prevention and treatment protocols that become standard of care for the ensuing decades.

In the area of pre-illness, simple cost-effective TCM disease-screening tools may help streamline the diagnostic supremacy of omics technology to be used in population disease screening. Conversely, the depth of diagnostic accuracy with omics technology will greatly boost the predictive power, which in turn can be used to validate some of TCM examination tools and practice pearls. For example, "omics" tools have made blood a window into health and disease and accurate stratification of illnesses or pre-illness for the opportunities to validate pre and post TCM intervention efficacies as they have often been criticized for not being able to ascertain efficacies in the absence of treatment randomization. One alternative to study randomization is through testing and stratification in large patient cohorts managed with different TCM interventions over long period of time and population based health outcomes were then recorded. TCM could also play ever increasing role in helping patients alleviate treatment related side effects or symptoms from these emerging immune based treatment. Some of the randomized trials had clearly validated the role of acupuncture in relieving cancer or cancer treatment related fatigue [32]. Convergence of patient-activated social networks, big data and their analytics, and systems medicine diagnostic tools will

provide adequate power to modernize, standardize and quantify the impact of personalized TCM treatment approaches versus reactive interventions. Physicians are also patients and engaging a stronger patient and physicians alliance will build greater trust, spread of digital health for greater information sharing and care process improvement. Past physicians giants all had experimented medicines on themselves before they prescribed to others. One hundred Persons Pioneers Project is a comprehensive scientific wellness including whole genomics, microbiome, immune, metabolome nutrition along with routine laboratory examination, sleep and activity monitoring. While the study was not directed by physicians but designed to collect data on scientific wellness. As discussed previously, virtually all "healthy" participants have some form of subclinical illness varying from nutrition, inflammation, to metabolism [13]. P4 medicine especially in the area of pre-illness represents the holy grail of medicine and was recognized as superior form of medicine dating back 4,000 years ago (Nei Jing or Internal Wisdom). Ancient TCM practitioners were rewarded for preventing diseases, and punished severely for missing the disease, forcing TCM practitioners to treat pre-ailment in the absence of today's laboratory and diagnostic tools for thousands of years. High profile media exposure of cupping for Michael Phelps in 2016 Olympic in Rio, dawn of cancer immunotherapy, genomic revolution and scientific diagnostics of pre-illness did not occur by co-incidence and will undoubtedly reinvigorate greater entry of P4 medicine with TCM practices into mainstream medicine. There are about 28,000 licensed TCM practitioners in the US and 400,000 TCM practitioners in China, a much smaller force as compared to the western based medical practitioners. Shifting to a proactive health care from reactive one will greatly boost the need for P4 medicine/TCM practitioners in the future. Collectively, we must then begin to test, interpret, upgrade and validate many of these long-held TCM tenets and principles, create and disseminate functional and system medicine curriculums to medical educators who can then bring back these new knowledge to next generation of physicians. TCM needs a universal scientifically interchangeable vocabulary to help implement future integrated research protocols on cancer treatment and prevention and reporting of disease outcomes per Good Clinical Practice Standard (GCP). For example, TCM long recognizes that cancer occurs as a result of energy imbalance in the blood particularly excessive or prolonged stress over long-term exposure to toxic chemicals in the form of pollutants in the air or water, toxins in food, and various drugs way before introduction of industrial alcohol and cigarettes production. TCM also believes that all toxic substances ingested are first processed in the digestive system. If toxins begin to build up and accumulate in the digestive systems and will lead to "stagnant chi" leading to carcinogenesis. A stagnant Chi in the modern medicine would indicate disrupted homeostasis in metabolism, immune surveillance, host inflammation, and neural hormonal regulation and there are simple Chinese vocabularies for each of the disrupted Chi recorded in the ancient TCM guidebook. Emergence of gut microbiome as one of the key driver for immune systems and disease represents a new tools for P4 medicine to partner with TCM practitioner to learn and test balance in host inflammation, immunes surveillance and psychosocial health.

For long time, stress and psycho-immunology is a new emerging field [32]. However, five elementary principles of TCM also recognize such important psychosocial link to the immune systems and define its links to internal organs and emotions centuries ago (Figure 1). Depressions are quite common in cancer patients especially in those with pancreatic cancer [34]. One of my favorite patients Melanie who had advanced pancreatic cancer is now a 10-year cancer free survivor. One of the key factors driving her survival may be in part due to our ever-positive psychosocial interactions in this wonderful ten-year doctor-patient journey. Cancer prevention and treatment that integrate depth of psychosocial interventions would for sure yield most impactful outcomes and author urges more in-depth testing and implementation of five healthy elements to tackle psychosocial aspects of healing process.

Simplified "Seed and Soil" theory in cancer prevention and treatment?

Ten cancer hallmarks can be summed up in a "seed and soil" theory proposed by Paget decades ago [35]. A small proportion of the cancer stem cells and its tumor microenvironment are responsible for cancer progression and death [36, 37]. Seed and soil theory has its simple element of truth when certain cancer traits were categorized into ten hallmarks: limitless cell proliferation and cell immortality (stemness), invasion metastasis and angiogenesis (epithelial mesenchymal transition seed-soil interface), and evasion of cell death through metabolism reprogramming, and immune destruction (soil) [38]. When one examine the seed and in soil in terms of five health elements (fire, vitality, energy oxygen), metal (immune shield and dormancy), wood (roots) earth (nutrient stroma) and water (nutrient, stroma) and these five elements are interconnected to internal organs as well as psychosocial aspect of one health (Figure 1).

A deeper understanding seed and soil theory and its ultimate to link to five basic health elements lead us to implement ADAPT (activating cancer stem cells from dormancy and potentiate targeting) strategy for patients with metastatic colorectal cancer using two agents capecitabine and celecoxib which had more than doubled median overall survival to 78.5 months

from 33 months) in patients with metastatic colorectal cancer also likely derived from reactivation of the immune surveillance mechanism [39].

Celecoxib is a designer drug targeting only COX-2 while sparing COX-1 for management of inflammation. Like aspirin, celecoxib can also prevent colorectal polyp in sporadic cases [40] as well as in patient with familial adenomatosis polyposis (FAP) in which patients suffered to have hundred of polyp during teenage years thanks to a dominant mutations in the APC genes [41]. This colon polyp prevention strategy led to uncovering of the cardiovascular toxicities related to the agent which can be predicted by examining five-health element (fire, angiogenesis or heart) which acts upstream of metal element (i.e. immune systems). Celecoxib like aspirin mediate cancer prevention through PGE2 and PD-1 pathway in the tumor microenvironment [24]. Following five-health element principles (Figure 1), P4 physicians and TCM practitioners can design and implement next generation personalized colorectal cancer prevention studies stratifying against known colorectal cancer risk factors (personal history, diabetes, inactivity, alcohol and smoking) in conjunction with genomic prediction tools and population based TCM screening and intervention tools against no personalized interventions. Combining the power of reductionist approaches, and systems principles of "seed and soil" and five elements may yield pleasant surprises in cancer prevention and treatment in the future.

Opportunities and Challenges of P4 medicine and TCM

We are living in an exciting era where power of immunotherapy, system medicine tools, and modern TCM tools and strategy and scientific wellness have now finally converged and is poised to transform future of cancer prevention and treatment. From the business perspective, this new health care network will be more integrative, cross disciplinary, and has in-depth knowhow of P4 systems medicine and TCM departing from the mainstream medicine discipline that continues to be one-on-one encounter to addressed reactively to a know ailment or illness. Time is ripe to devise a new generation TCM based Framingham style personalized cancer prevention program ideally assisted by artificial intelligence programming that can assimilate literatures cancer immunology, predictive diagnostics, and TCM intervention tools leading to industrialization of treatment standard that be duplicated despite the genetic and phenotypic diversities of the health care consumers and heterogeneities of physicians and TCM workforce [42].

Transformation of medicine will not occur overnight as stakeholders in the established medical systems have been entrenched in these reactive medical systems for decades. Two major challenges to achieving P4 medicine--technical and societal barriers--and the societal barriers will prove the most challenging. How do we bring patients, physicians and members of the health-care community into alignment with the enormous opportunities of P4 medicine? In part, this will be done by the creation of new types of strategic partnerships--between patients, large clinical centers, consortia of clinical centers and patient-advocate groups. For some clinical trials it will be necessary to recruit very large numbers of patients--and one powerful approach to this challenge is the crowd-sourced recruitment of patients by bringing large clinical centers together with patient-advocate groups.

We are in a historical moment to bring "omics" technology for early pre-illness and pre-cancer detection and intervention. We will need challenge and revise and improve and validate the previously established TCM principles through the use "omics" technology and knowledge from stem cells biology and cancer immunology. Many legitimate questions remain: 1). Will interventions of these actionable items improve health and quality of life and ultimately longevity? 2). Can nutrition or none drug intervention be impactful for the long-term health care outcomes? 3) How do we approach certain genetic or enzymatic deficiencies 4) What are the best intervals for repeated laboratory testing and medical checkups? 5). Will be people having information overload and created unnecessary fear when tested for their genomes and microbiome? 6). How do we get more physicians to embrace the proactive living instead? 7) Can this be used to prevent and diagnose deadliest disease like cancer or heart disease or Alzheimer disease? We believe that P4 medicine armed with diagnostic tools and best of TCM will be able to transform the medicine landscape especially in the area of pre-illnesses intervention. We propose to form a P4 medicine alliance combining the best of western medicine and TCM to zeroing in on pre-illness or disease risk factors for effective intervention. In the colorectal cancer risk factors, there are known genetic predisposition familial adenoma polyposis (FAP) and hereditary none polyposis syndrome (HNPCC) in a subset of individuals with family history but majority of the patients at risks are those with associated risk factors includes diabetes, obesity, inactivity, excessive alcohol, smoking, poor dietary habit and consumption of smoke products, race and poor socioeconomic status. Human as well as animal kingdom all desire for longevity free of illnesses or suffering. Animal kingdom does it by natural selection and by ensuring that best genes and behavioral trait are passed to the next generation Mankind has greater freedom and luxury to indulge in many of our good and risky behaviors ranging from consuming "bad" versus healthy food products to cigarette or alcohol

consumption that ultimately threaten our health on many different dimensions.

In summary, population based deafness screening program by Capitalbio in China had already reached a 1 million children milestone. This population based genetic screening program will eliminate iatrogenic deafness in children akin to the successful various vaccines program that had eliminated many of the deadly viruses such as smallpox or polio, hepatitis B. For cancer prevention, however, best strategies are to implement a individual initiated family based cancer prevention plans ideally starting in early age and through his or her adulthood. This would include a guided dietary and exercise program and life-long good behavior modifications. A team effort from Dr. Daniel Amen and reverend Rick Warren were able to help 30,000 Saddleback members collectively shedding ~226,000 kg for in six-month with no medical intervention. With the alarming cancer epidemics in China, we will need to build a trans-disciplinary healthcare team to execute strategies that can go beyond the Saddleback success and turn physicians and TCM physicians to future pioneers in this consumers oriented health care movement, leading themselves and their families to a better wellness and health path of life time. AI that stored all relevant scientific data in an easily retrievable virtual health cloud [38] can produce real time actionable health solutions and plans for individuals and families continuously. The day that health conscious consumers will be shifting en mass to this innovative home-based health and wellness solutions from the current reactive health care model is upon us before we know it.

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