

16 August 2011 (Tuesday)

## Track 4(ii)

### 4(ii): Chemoprevention

#### Session Chair

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#### Session Co-Chair

**Dr. Jaime A. Yáñez**

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### Session Introduction

**Title:** Mechanistic studies of the bioavailability barrier network (BBN) and its negative impact on the disposition and chemopreventative efficacy of dietary phytochemicals

Dr. Stephen W.J. Wang, Millennium Pharmaceuticals Inc., USA



**Title:** Bioreactive compounds for cancer chemoprevention

Dr. Jaime A. Yáñez, Alcon Laboratories Inc., USA



**Title:** Beyond the pyramid: Diet and alternative compounds for cancer prevention

Dr. Jeffery G. Herman, University of California San Francisco, USA



**Title:** What do you mean I can't take my vitamins anymore? A qualitative review of nutritional supplement use during cancer treatment

Dr. Alina Barnett, University of California San Francisco, USA



## Mechanistic Studies of the Bioavailability Barrier Network (BBN) and its Negative Impact on the Disposition and Chemopreventative Efficacy of Dietary Phytochemicals

Stephen W.J. Wang

Drug Metabolism and Pharmacokinetics, Millennium Pharmaceuticals Inc, USA

Polyhydroxylated phytochemicals such as flavonoids, isoflavonoids and resveratrol have received major attention for their abilities to decrease the risk of coronary heart disease, ischemic stroke and most importantly prevent various forms of cancer including but not limited to colorectal and lung. However, a major conundrum observed in the clinic is that these chemopreventative phytochemicals all have extremely poor bioavailability.

To investigate the mechanisms in which our body can limit the amount of phytochemicals in the systemic circulation, we investigated the disposition of phytochemicals in four aspects of 1) absorption 2) distribution 3) metabolism and 4) excretion/elimination. Utilization of in vitro (e.g., ATPase assays, Cell lines, Vesicular transport assays), in situ (simultaneous 4-intestinal site perfusion models) and in vivo (e.g., knockout animals) methods as well as modeling & simulation (i.e., PBPK), we have discovered a barrier network which explains this observed phenomenon. Overall, this barrier network is not only governed by the following: 1) metabolism of these phytochemicals (typically phase II) 2) elimination of metabolites utilizing active transporting proteins (ABC efflux transporters) but is also dependent on the interaction between these two steps. This mechanism of coupling is extremely important as it governs the dispositional process of phytochemicals.

However, additional complexities are introduced as we attempt to disrupt this coupling process and observe an unexpected compensation via other proteins (both metabolic and transporters) within the same superfamily. Therefore, we propose here a bioavailability barrier network worthy of further characterization in order to better understand the disposition of phytochemicals.

### Biography

Dr. Stephen Wang received his training in pharmaceutical sciences at the Texas Medical Center under Professor Ming Hu. Dr. Wang currently serves as a principal scientist in the department of Drug Metabolism and Pharmacokinetics at Millennium Pharmaceuticals in Cambridge MA. Previously, Dr. Wang served as a senior scientist in the department of Drug Metabolism and Pharmacokinetics at Merck. Dr. Wang's research interests focus on the disposition of xenobiotics in an effort to improve bioavailability of chemopreventive agents. Dr. Wang has made significant contributions in the field with a consistent publication track record of over 25 manuscripts in peer-reviewed scientific journals and various book chapters.

## Bioactive Compounds for Cancer Prevention

**Jaime A Yáñez**

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Consumption of bioactive compounds could be close to 1 g/day in our diet, making them the largest source of anti-oxidants. Dietary sources include fruits, vegetables, cereals, legumes, chocolate, and plant based beverages such as juices, tea, and wine. Extensive biomedical evidence suggests that bioactive compounds no matter their class may contribute to the prevention of cardiovascular disease, cancer, osteoporosis, diabetes, and neurodegenerative diseases. They have been also shown to exhibit beneficial effects on capillary permeability and fragility, to have anti-platelet, hypolipidemic, anti-hypertensive, anti-microbial, anti-viral, anti-allergenic, anti-ulcerogenic, cytotoxic, anti-neoplastic, anti-inflammatory, anti-atherogenic, and anti-hepatotoxic activities. These potential health benefiting properties may call for development of these compounds into future therapeutic agents. The content of bioactive compounds is also potentially influenced by food processing and storage conditions, which can result in transformation of flavonoids, and loss of flavonoid content. This presentation will briefly cover some relevant current statistics about cancer, dietary recommendations and the different family of bioactive compounds that have exhibited chemopreventive properties in selected foods coverings pre-clinical and clinical studies that have been performed to identify their potential chemopreventive effects after dietary consumption.

### Biography

Dr. Yáñez received his Ph.D. in Pharmacology and Toxicology from Washington State University on 2008. His graduate research centered on stereospecific bioanalytical, pharmacokinetics and pharmacodynamics of chiral flavonoids. After graduating he joined Schering-Plough (later Merck) where he worked in the DMPK Biodisposition group working mainly with HCV drugs PK studies and in-silico modeling in order to bring GastroPlus into the Biodisposition group. He currently works for Alcon where he works with various glaucoma and intraocular pressure (IOP)-lowering agents and closely works with regulatory submissions in the DMPK department. He continues his research interests on PK/PD, bioactive compounds and health effect of various traditional plants. For this, he collaborates with various universities in Peru and Spain where he serves as research consultant, reviewer for grant submissions, and provides seminars in various subjects. Dr. Yáñez is member of various scientific and honor societies in the US, Europe and Latin America. He has about 50 peer-reviewed reviews, articles, and books chapters.

## Beyond the Pyramid: Diet and Alternative Compounds for Cancer Prevention

**Jeffery G. Herman**

University of California San Francisco, USA

Personal dietary choices have long-term health consequences, with important roles in disease development and incidence including heart disease, diabetes, and cancer. It is estimated that 30-40% of all cancers can actually be prevented by adopting a well-balanced diet and other healthy lifestyle choices (e.g. reduced stress, increased exercise). The scope of dietary intervention research with regards to cancer prevention and treatment is large; ranging from dietary restriction such as specific amino acid restriction (tyrosine/phenylalanine) to dietary supplementation including curcumin and saw palmetto.

In the past, nutritional experiments have largely focused on the relative immediate effects of dietary intervention with regards to alterations of important signaling pathways. These experiments have often exhibited moderate and somewhat inconclusive effects in vitro, in vivo, and in the clinic; however, as new innovative research is beginning to illustrate, dietary intervention is not strictly about immediate and direct effects. Through the alteration of essential protein, genetic and epigenetic expression, the effect of diet and nutrition on cancer and disease incidence is subtle with long-term consequences which can span generations. By understanding these subtle dietary effects with regards to overall health, novel biomarkers for cancer incidence may be discovered and novel drug targets could be developed.

In order to achieve a truly successful use of diet in the prevention of cancer, we must move beyond laboratory and clinical research, and also begin to focus on dietary education, of patients, the general public and the medical community.

### Biography

Dr. Jeffery Herman achieved his PhD in Pharmacology/Toxicology from the Washington State University under the mentorship of Dr. Gary G Meadows. Dr. Herman has worked at top research facilities including Oregon Health Science University and San Francisco Veteran Affairs Medical Center/University of California San Francisco. Dr. Herman's research interests largely lie in the role of dietary and nutritional intervention of cancer and other diseases. Dr. Herman has published papers in peer reviewed scientific journals, maintains a successful science and nutrition website and is an active science/medical writer.

## What Do You Mean I Can't Take My Vitamins Anymore? A Qualitative Review of Nutritional Supplement Use During Cancer Treatment

**Alina Barnett**

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Complementary and alternative medicine (CAM) and over-the-counter (OTC) drug use among patients undergoing chemotherapy is increasingly prevalent with estimates reaching nearly fifty percent. Studies suggest that health care professionals rarely have complete medication lists on file for patients receiving chemotherapy. Concomitant OTC and CAM use during chemotherapy could potentially lead to severe drug interactions; a problem that is compounded when health care professionals are unaware of patient non-prescribed or alternative therapy use. The present study provides a literature review of both OTC and CAM use by patients undergoing chemotherapy as well as healthcare professional perception regarding patient OTC and CAM preferences. Non-disclosure of CAM and OTC use is postulated to occur for a variety of reasons: (1) a patient perception that healthcare professionals are displeased with alternate therapies, (2) misleading OTC packaging and (3) misunderstandings of the possible dangers that OTC and CAM products can cause regarding potentially severe interactions with chemotherapy. Understanding patient motivation to use CAM and OTC products during chemotherapy could improve open communication between patients and healthcare providers. Patient disclosure of OTC and CAM use to pertinent healthcare providers during clinic visits as well as more thorough documentation of all medications, would allow for an accurate medication list that may reduce potential drug interactions during chemotherapy.

### Biography

Dr. Alina Barnett completed her Doctor of Pharmacy degree at Washington State University and is a Pediatric Clinical Pharmacist at UCSF Benioff Children's Hospital and an Assistant Clinical Professor at UCSF School of Pharmacy. Dr. Barnett's research interests lie in effective medication counseling in the adolescent oncology and transplant patient and innovative clinical pharmacy teaching techniques.