



Keynote Lecture XV

Breast Cancer Etiology: Diet, Hormones, and Genes

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Dr Wei Zheng received his graduate training in epidemiology from the Shanghai Medical University, Johns Hopkins University, and National Cancer Institute and received an MPH in 1986 and a PhD in 1992. He was a faculty member at the University of Minnesota from 1993 to 1997 and was then appointed in 1998 as a full professor at the University of South Carolina. Since 2000, Dr Zheng has been a tenured professor and the Director of Epidemiology at the Department of Medicine, Vanderbilt University School of Medicine. In 2002, he was awarded an endowed professorship and appointed as an Ingram Professor of Cancer Research and the Co-leader of the Breast Cancer Research Program at the Vanderbilt-Ingram Cancer Center.

Dr Zheng's main research has focused on the molecular and nutritional epidemiology of cancer and the evaluation of the predictive value of biomarkers in cancer diagnosis and progression. Using a population-based approach, Dr Zheng's group is investigating genetic and dietary factors as well as their interactions with the risk of cancer and other common chronic diseases. His group has published some of the first research papers on the role of certain genetic and dietary factors in the etiology of breast cancer.

Dr Zheng has published over 180 research papers. Currently, he is the Principle Investigator for six large epidemiological studies funded by the NIH. Dr Zheng has served regularly on NIH committees reviewing research grant applications. He is a member of the editorial board for Cancer Epidemiology, Biomarkers & Prevention and a reviewer for many epidemiology and cancer journals.

Breast cancer is one of the most common malignancies in women around the world. Over the past few decades, there has been an alarming increase in the incidence of this cancer among Chinese women living in several parts of the world, including Shanghai. In 1996, we launched a large epidemiological study – the Shanghai Breast Cancer Study – to comprehensively investigate etiological factors for breast cancer and explore possible reasons for the increase of this malignancy among women in Shanghai. Approximately 1500 incident cases and 1500 community controls were recruited into the study between 1996 and 1998. Starting in 2001, a second set of 3000 cases and controls are being recruited to enhance the statistical power of evaluations of gene-gene and gene-environment interactions in breast cancer risk. In-person interviews were conducted to collect exposure information, and biological samples were collected to evaluate biomarkers. Multivariate analyses were performed to evaluate the association of breast cancer risk with study variables.

Over 60 research papers have been published from the Shanghai Breast Cancer Study, addressing various hypotheses of breast cancer risk and survival. Major lifestyle factors identified with an increased risk of breast cancer include low intake of soy foods in adolescence and adulthood; low intake of folate and certain fruits and vegetables; high intake of meats, particularly well-done meat; low level of physical activity; and high body weight and central obesity. Several biomarkers have been found to be related to the risk of breast cancer, including blood steroid sex hormones, IGFs, and C-peptide, urinary isoflavones, isothiocyanates, estrogen metabolite ratios, and cortisol ratios, and several genetic markers. Approximately 100



polymorphisms in over 30 candidate genes have been analyzed in the study. Apparent gene effects for several polymorphisms have been identified, including those located in the *ESR1*, *ESR2*, *CYP11A*, *CYP11A1*, *GSTP1*, *SHBG*, *SULT1A1*, *IGF1*, *IGFBP3*, *IGF1R*, *ALS*, *INS*, *VEGF*, *CCND1*, and *STK15* genes. Several genetic polymorphisms have also shown evidence for interactions with other genes and/or lifestyle factors, including those in genes, such as *MTHFR* and *NQO1*, that show no major gene effects by themselves. The results from the Shanghai Breast Cancer Study indicate that multiple factors are involved in the etiology of breast cancer, and improving understanding of these risk factors will be valuable in designing cost-effective strategies in the prevention of this common malignancy.