

FINDINGS ON THE BENEFITS OF GREEN TEA ARE THE LATEST EXAMPLE OF ONE FACULTY MEMBER'S APPLICATION OF MOLECULAR EPIDEMIOLOGY TOWARD HIS PASSION SINCE SERVING AS A "BAREFOOT DOCTOR" IN CHINA: DISEASE PREVENTION.



Zuo-Feng Zhang:

New Science, Old Goals

Zuo-Feng Zhang was 16 when he arrived on the Nantong Farm one chilly spring day in 1969 for the beginning of a four-year assignment. His native China was in the midst of Mao Tse-Tung's Cultural Revolution, and Zhang was one of more than 1 million students sent to the countryside to accept "re-education." He was then chosen by farmers as a "barefoot doctor" to bring basic preventive medicine to the poor. "It was a basic network to treat the farmers in remote rural areas," he explains. "The farmers would choose a student they trusted, then the student would go to a mid-level hospital for three months of training and come back as a doctor."

More than three decades later, Zhang's base of operations has moved to Westwood, Calif., and the UCLA School of Public Health. Rather than treating Chinese peasants for diarrhea, colds and other common ailments, he's using the latest techniques in the emerging field of molecular epidemiology to hunt for tumor markers and identify genetic mutations, inherited susceptibilities, and the like.

He'll acknowledge that more than just time and distance separate what he does today from what he was doing 30 years ago. But the way Zhang sees it, his primary goal — preventing disease — has remained rock-steady.

As a cancer molecular epidemiologist, though, his work affects far more people. A case in point is his recent finding — widely publicized around the world — that green tea has a protective effect against stomach

cancer and chronic gastritis. Though the rates are lower in the United States, stomach cancer remains the second-most common malignancy internationally — and the most common cancer among both sexes in China, where 38% of the world's cases occur. Green tea is particularly popular in Asian countries. While previous studies had looked at possible health benefits of green tea in that part of the world, they had found little; Zhang suspects this may be because consumers of green tea are often also heavy consumers of alcohol and tobacco.

Zhang conducted a population-based case-control study where the incidence of mortality from stomach cancer is highest — on the small island of Yangzhong, China, situated on the Yangtze River in Jiangsu Province. After adjusting for age, gender, education, body mass index, and levels of smoking and alcohol consumption, green tea drinkers had a 48% lower risk of stomach cancer than non-drinkers, and a 51% lower risk of chronic gastritis.

“Green tea seems to have several important anti-cancer properties,” Zhang says. “All tea comes from the same plant — *Camellia sinensis*. Certain chemicals in that plant, known as polyphenols, appear to have antioxidative activities.” (No such luck for black tea drinkers — the majority of tea consumers in the United States. Zhang notes that black tea loses many of its polyphenols in the fermentation process.)

The results of the study, published in the *International Journal of Cancer*, did more than boost sales of green tea (one can even find a green-tea specialty shop in Westwood these days). It also set Zhang and colleagues on a hunt for so-called tumor markers — early genetic changes that, in this case, would foreshadow stomach cancer development. Indeed, Zhang's aim in population-based studies such as the one involving green tea and another, similarly well-publicized paper in which Zhang linked smoking marijuana to increased risk of head and neck cancers is to illuminate in greater detail the sequence of events that lead to cancer. Understanding these molecular changes would help researchers intervene at a more curable stage, or before malignancy ever takes hold.

“Traditional epidemiological studies have looked at the correlation between risk factors and disease — to show, for example, that smoking is linked to cancer,” Zhang says. “But we don't know exactly how that process occurs. We know that smokers are much more susceptible to certain cancers than non-smokers, but we don't know why.” Nor is it clear why some

risk-takers are more susceptible to disease than others. Why, for example, do some heavy smokers live to be 90 while 10-year smokers die of lung cancer in their 50s?

As a molecular epidemiologist, Zhang looks at intermediate steps between exposure and disease, including the amount of exposure to the carcinogen, the effect of a given dose on the target tissue, the inherited susceptibility to cancer, the link between environmental exposures and gene mutations, and the gene-environment interaction that produces clinical disease and affects prognostic factors.

How did a former barefoot doctor get to this point? Zhang believes it was a natural progression. After his four years at Nantong Farm, he attended Yangzhou Secondary School of Hygiene, where he earned a diploma in public health. He then worked for three years as an infectious disease epidemiologist in the Schistosomiasis Control Program in Yangzhou. In 1978 he began five years of medical school at Shanghai Medical University, followed by two years of an M.P.H. program in cancer epidemiology and then another two years toward his Ph.D., all at Shanghai. Zhang came to the United States in 1988 and obtained his Ph.D. from the State University of New York at Buffalo in 1991. He has been on the UCLA School of Public Health faculty since 1997.

In his final year of medical school, Zhang's rotation took him to an area with an extremely high rate of liver cancer. “I saw people in their 30s and 40s dying of this disease every day, and I realized there was nothing that could be done for them,” he says. “That's when I decided to devote my career to working in preventive medicine.”

Much excitement surrounds the field of molecular epidemiology, given the sequencing of the human genome and the powerful tools that are being developed to enable multi-gene studies aimed at identifying the biological underpinnings of diseases. But Zhang's public health focus distinguishes his work from that of many of his molecular biology colleagues.

“Using this new genetic knowledge for public health and environmental health science is very important,” he says. “Clinical scientists are interested in genes that can predict the outcome of disease related to the decision on treatment of the patient. We're interested in using molecular genetics to *prevent* the disease.

“Prevention is what I've always done, even when I was a barefoot doctor. It's just that now the techniques look different, and my patients are entire populations.”



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—Dr. Zuo-Feng Zhang