

Shiuan Chen, Ph.D.
Director, Department of Surgical Research

Dr. Chen received his Ph.D. in Biochemistry from the University of Hawaii in 1977. In 1982, he was recruited by the University of Southern California as a Research Assistant Professor. Dr. Chen joined the Beckman Research Institute of the City of Hope in 1985 and was subsequently promoted to Professor in 1994. In 2002, he was appointed as the Director of the Department of Surgical Research. He leads the scientific program for the Division of Surgery, oversees the current surgical research activities and help plan future programs.

A major research focus of Dr. Chen's laboratory is to investigate the roles of aromatase in breast cancer development. In estrogen-dependent breast tumors, estrogen binds to the estrogen receptor protein and induces the expression of peptide growth factors that are responsible for the proliferative responses of cancer cells. Aromatase is an enzyme that converts androgen to estrogen. Since aromatase is the enzyme responsible for the synthesis of estrogen, and estrogen can have a major effect in the development of breast cancer, an abnormal expression of aromatase in breast cancer cells and/or surrounding adipose stromal cells may have a significant influence in breast tumor development and growth in cancer patients. Aromatase is expressed at higher levels in human breast cancer tissue than in normal breast tissue, as measured by various biochemical assays. Studies are being conducted to analyze the tissue specific regulation of the promoter elements in the human aromatase gene. Furthermore, structure-function studies are performed in this laboratory to characterize the structural features of the active site of aromatase. Since the suppression of estrogen formation (with aromatase inhibitors) is considered an important breast cancer treatment strategy, it is vital that the structural nature of the inhibitor-binding site of aromatase be determined. This information will be critical for designing potent and selective aromatase inhibitors for breast cancer treatment.

Dr. Chen and his colleagues also carry out research to determine how environmental chemicals modulate the activity and expression of aromatase in human tissue. Experiments are being carried out to provide a molecular and mechanistic basis as to how phytochemicals and organochlorine compounds affect estrogen biosynthesis (i.e., aromatase function) in women. Dr. Chen's laboratory has found that grapes, mushrooms, and red wine contain chemicals that can suppress aromatase activity. Therefore, a diet that includes grapes, mushrooms, and red wine would be considered preventative against breast cancer. He and his colleagues are purifying and characterizing these natural anti-aromatase chemicals and evaluating their *in vivo* effects using animal experiments.

Furthermore, Dr. Chen has found that mushrooms contain chemicals acting as inhibitors of steroid 5-alpha reductase. Androgen plays a critical role in prostate cancer development. In the prostate, testosterone (an androgen) is converted to dihydrotestosterone (DHT), an androgen that is more potent than testosterone. This conversion is catalyzed by the enzyme steroid 5-alpha reductase. An elevation of the steroid 5-alpha reductase activity in prostate may cause benign prostate hyperplasia (a common problem in older men) and promote the growth of prostate cancer.

Inhibitors of steroid-5-alpha reductase have been developed to treat these prostate diseases. Dr. Chen's laboratory is purifying the chemicals from mushrooms and designing animal experiments to evaluate the use of these phytochemicals as drugs in the prevention or treatment of prostate cancer.

In addition, Dr. Chen's laboratory has identified a novel co-regulatory protein (i.e., PNRC) that modulates nuclear receptor-mediated and Ras/MAP kinase-mediated pathways by interacting with nuclear receptors and GRB2. Extensive molecular studies are being performed to determine the molecular features of this protein for its interaction with proteins in the signal transduction pathways.

Dr. Chen's research work is being supported by grants from NIH, California Breast Cancer Research Program and the American Institute for Cancer Research. He has authored more than 130 published articles. He has been a member of the City of Hope Cancer Center since 1985. He has been invited to serve as a member of numerous grant review panels by the NIH, the US Army Breast Cancer Research Program, the US Environmental Protection Agency, and the American Heart Association. He also holds the position of Corresponding Editor for the Journal of Steroid Biochemistry and Molecular Biology.