

## Single Nucleotide Polymorphisms affecting Drug Response in Cancer Chemotherapy

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Advances in our understanding of therapy for breast cancer has come slowly, but the overall mortality from the disease has been unaltered for several decades. Therefore the aim of our investigation has been to understand the genetic basis of the response to chemotherapy in breast cancer patients. However, developments in the past decade have given cause for new but cautious, optimism for patients. These important developments have come primarily from basic research in drug-gene interactions that has led to testable hypotheses regarding new approaches like the one described here for drug metabolizing genes. We have studied three genes (MTHFR, DPD and TS) in the general treatment regime pathway and another two genes (CYP2D6 and SULT1A1) involved in hormone therapy.

The biotransformation of tamoxifen is mediated by cytochrome P450 enzymes mainly through demethylation and hydroxylation to form several primary metabolites, principally 4-OH-tamoxifen, alpha-OH-tamoxifen, *N*-desmethyltamoxifen, and 4-OH-*N*-desmethyl-tamoxifen. 4-OH-tamoxifen is considered to be a more potent anti-oestrogen than the mother substance and is capable of binding the ER with greater affinity. From experimental studies it has been shown that the transformation of tamoxifen into 4-OH-tamoxifen is mainly catalysed by the liver enzyme CYP2D6. SNP studies in this gene revealed its role in modulating the effect of anti-neoplastic drugs. We describe here the genetic basis for inter-individual differences in drug response and emphasize the need to use such genetic information to predict the safety, toxicity, and/or efficacy of drugs in individual patients or groups of patients. Polymorphisms in genes encoding drug-metabolizing enzymes, drug transporters and drug targets can be used to predict toxicity and response to pharmacologic agents used in breast cancer treatment.

### Biography:

Dr. Kaiser Jamil is Principle Investigator and the Head of Genetics Department, having published more than 250 papers in journals of repute and guided 25 scholars for PhD degree. During the last decade following her instincts, she has taken up several projects related to human health, for 'War against Cancer' she has contributed in the field of Biomarkers in Breast cancer, Leukaemia, and Head and Neck cancer. Her work on SNPs of drug metabolizing genes in cancers has been published in peer reviewed journals, unfolding the mechanisms of several genes and other genes which network with these genes, elucidated Drug-Gene interactions. She has also contributed on the role of some signalling pathways such as tyrosine kinase inhibitors (TKI) and MAPK in haematological malignancies and HNC. Her research continues to unravel genotypes leading towards personalised medicine.