Recent advances in molecular biology and genetics have made it possible to assess the role of gene-environment interaction in the process of chemical carcinogenesis. Epidemiological studies of exposure and molecular etiology of human carcinogenesis are fast emerging as reliable and promising tools for cancer risk assessment.

Studies that incorporate the use of different biological markers of susceptibility in human populations are often referred to as molecular epidemiological studies. Environmental carcinogens contained in polluted air, such as polycyclic aromatic hydrocarbons, aromatic amines or N-nitroso compounds, predominantly form DNA adducts but can also generate inter-strand cross-links and reactive oxygen species. If unrepaired, such lesions increase the risk of somatic mutations and cancer.

Lung cancer is considered to be the end-stage of multistep process of carcinogenesis. Lung carcinogenesis in humans requires exposure to environmental agents, including the inhalation of tobacco smoke, radioactive compounds, asbestos, heavy metals, and petrochemicals. Genetic damage caused by chronic exposure to carcinogens e.g., those in cigarette smoke, probably is the driving force behind the multistep process. Suggestive evidence of genetic damage is the association of cigarette smoking with the formation of the DNA adducts in human lung tissue. Carcinogenic compounds in tobacco smoke include the polynuclear aromatic hydrocarbons (PAHs), including the classical carcinogen benzo[a]pyrene (BaP), and the nicotine-derived tobacco-specific nitrosamine, 4-(methylamino)-1-(3-pyridyl)-1-butanone (NNK). Although the chemical constituents of tobacco smoke have been described, the specific constituents that most influence carcinogenesis remain poorly understood. A number of metabolic enzymes responsible for bio-activation and detoxification of environmental chemicals, carcinogen-induced DNA adducts and
chromosomal aberrations, and host DNA repair capacity have been measured in human peripheral lymphocytes. Several biomarkers for genetic susceptibility to lung cancer have been developed and validated in pilot studies that have demonstrated their association with increased risk of lung cancer. These markers allow estimation of inter-individual variations in response to carcinogen exposure and thus assessment of cancer risk. Several biomarkers for genetic susceptibility to lung cancer have been developed and validated in pilot studies that have demonstrated their association with increased risk of lung cancer. Metabolic polymorphisms, leading to different ability to metabolize carcinogens either through activation or detoxification stages, appear to be an important set of genetically influenced traits associated with variability in the risk of lung cancer. Both Phase I and Phase II metabolizing enzymes are under the control of polymorphic genes. Besides the potential of DNA repair genes (being polymorphic) also contribute to this variability.

The present study was designed to study the distribution of metabolic genes \textit{CYP1A2}, \textit{NAT2} and \textit{SULT1A1} on the risk of lung cancer in North Indian Population. These genes are involved in the metabolic activation and detoxification of aromatic amines. As human exposure to environmental and tobacco smoke occurs primarily via the respiratory tract, expression of \textit{CYPs}, \textit{NATs} and \textit{SULTs} in respiratory tissues may contribute significantly and specifically to the metabolic activation of aromatic amines and their metabolites. The DNA repair gene \textit{XRCC1} was also included to assess the impact of polymorphism of this gene on susceptibility to lung cancer. The present study was aimed at identifying groups of individuals who are at greatest risk of developing lung cancer. The goal of study was to fulfill the promise of preventive medicine: prevention and control of disease and the data obtained in the work is the first of its kind on these genes in Indian population and will form a basis for exploration with a large number of samples.
This study was carried out during the study leave sanctioned to me by the Govt. of India thereby giving me an opportunity to undertake this study. I am extremely thankful to the Government for the same.

I take this opportunity to express deep sense of gratitude to my esteemed and generous guide Dr. R.C. Sobti, MSc (Hons. Sch.), Ph.D, F.N.A.Sc., F.A.M.S., F.Z.S., F.P.A.S., F.S.C.G., Professor, Department of Biotechnology, Panjab University, Chandigarh for suggesting to me the problem, his benevolent supervision, constant encouragement, invaluable suggestions and sincere interest in this study.

I also extend my heartfelt gratitude to Dr S.K Gupta. Former Head of the Department of Pharmacology, AIIMS, New Delhi for his guidance and Dr Sanjeev Sinha, Assistant Professor, Department of Medicine AIIMS, New Delhi for providing to me the clinical samples for the study.

I would also like to thank the Indian Council of Medical Research (ICMR) for funding the larger study of which my study was a part.

I would especially like to thank the faculty and the technical staff of the Department of Biotechnology for their constant moral support, critical suggestions and for providing to me facilities for conducting the study. It is my privilege to specially thank Mr Navtej for his help in photographic work.

I am glad to convey my heartfelt gratitude to all my colleagues especially Siddharth Sharma, Amit Joshi, Pushpinder Kaur and Jagmohan Singh for their constant support and fruitful discussions.

Last but not the least, I would like to acknowledge my family: parents for their unfailing support; husband for his patience and confidence in me; sons Arul and Arnav for their cooperation throughout the study.

Dated: Feb. 2006

Suparna S. Pachouri