Globally, cancer is the leading cause of premature morbidity and mortality in the developed countries. Based on current projections, cancer deaths will continue to rise, with nine million people estimated to die from the disease in 2015, and more than 11 million in 2030 (Gavhane et al., 2011). Because cancer disproportionately affects the elderly, economic burden due to it will become an even greater concern in future as a result of the ageing “baby boomer” population.

Lung cancer is a major global health concern and will remain so for many years to come. During the last 30 years, significant advances have been made with regard to understanding the mechanisms of lung carcinogenesis. These advances have not been paralleled by comparable advances in its treatment and cure (Weir et al., 2003). One important factor that has impeded progress in clinical oncology is the complexity of lung cancer as disease; each tumor type consists of a large number of sub-types that differ with regard to their spectrum of genetic alterations. Each molecular subtype may be associated with a distinct clinical behavior and the treatment response (Hayes et al., 2012). Detection of lung cancer at an early disease stage is critical for successful clinical therapy, an improved prognosis, and increased survival rate. Over a last decade, intense interest has been focused on tumor-specific biomarker discovery and their clinical uses. This interest is accelerated by the completion of human genome project and the progress of techniques in proteomics. Protein biomarkers can be more accurate signatures of a disease state than DNA biomarkers since proteins and not transcripts are the actual functional players (Stroncek et al., 2005; Karley et al., 2011). Neuron-specific enolase, carcinoembryonic antigens, cytokeratin 19 fragments, and some other proteins are the most commonly used lung cancer markers (Park et al., 2011). However, only few of these markers are useful in a routine clinical setting, owing to their limited sensitivities and specificities, thus underscoring the need for new clinically relevant sources. The blood contains a treasure trove of previously unstudied biomarkers released from cell, tissue or organism through classical and non-classical secretion that could reflect the ongoing physiological state of all tissues including tumor tissues (Xue et al., 2008). These secreted proteins may be growth factors, extracellular matrix-degrading proteinases, cell motility factors and immuno-regulatory cytokines or other bioactive molecules. They are essential in the processes of differentiation, invasion, metastasis and angiogenesis of cancers by regulating cell-to-cell and cell-to-extracellular matrix interactions. The human serum proteome (secretome) can be non-invasively measured and it provides a tremendous opportunity for detecting, therapeutic monitoring, and deciphering basic cancer mechanisms. However, it is difficult to analyze blood serum because it comprises large amounts of
albumin and a wide dynamic range of other heterogenic proteins that masks the lower abundant proteins useful as specific biomarkers. While, two dimensional electrophoresis and mass spectrometry are powerful high throughput analytical techniques to cancer identification that yields comprehensive peptide and protein serum profiles by proteome complexity reduction, novel proteomic approaches like ICAT, iTRAQ, SILAC and others make it possible to compare the expression of hundreds of proteins in several samples in a single experiment (Phanstiel et al., 2011; Boisvert et al., 2012; Geiger et al., 2012). The continuous development in quantitative proteomic methods, as well as advanced bioinformatics for data handling and interpretation, has brought with it the hope of discovering novel biomarkers that represent the powerful tools in disease diagnosis, predicting susceptibility, monitoring progression and gauging the effects of novel therapeutic agents.

Smoking and a number of constituents of tobacco are responsible for development of lung tumors, however the deleterious effects of tobacco derived carcinogen, nitrosamine 4-(methylNitrosoamino)-1-(3-pyridyl)-1-butanone (NNK, nicotine derived nitrosamine ketone) remain unmatched (Hecht, 2008). Mutagens and carcinogens present in tobacco smoke are capable of producing free radicals and reactive oxygen species in excess that initiate and promote oxidative damage to DNA and alter gene expression. The potential cellular damage is the disturbance in the prooxidant–antioxidant balance in favor of the former. Therefore, investigating antioxidant depletion as a biomarker of oxidative stress involving assessment of decreases in antioxidant concentrations or increases in their metabolites have the potential to help establish pathogenic stages of lung cancer and inform outcome measures of clinical trials (Burlakova et al., 2010; Small et al., 2012).

Spontaneous lung tumors in rats are similar in morphology, histopathology and molecular characteristics to human adenocarcinomas. Rat models for lung cancer can thus serve as a valuable tool not only for understanding the basic lung tumor biology but also for the development and validation of new tumor intervention strategies as well as for the identification of markers for early diagnosis (De Seranno and Meuwissen, 2010).

It is pertinent for a candidate biomarker to survive the journey from bench to bedside. Validation of candidate biomarkers has a single goal: to determine, if there is sufficient evidence for a potential clinical utility of a given biomarker candidate to ensure further investment in that candidate for
clinical trials. A validation is therefore essential before moving forward with this potential biomarker candidate.

**Hence, in the background of above facts the main objectives undertaken for my PhD. work were:**

- To develop an experimental rodent model for study of lung cancer.
- To understand the inter-relationship between lung cancer and stress by monitoring the alterations in the level of stress-related enzymes at regular intervals.
- To study serum specific protein expression profile in control and diseased animals using 1D and 2D analysis.
- To identify and purify the novel protein that can be used as potential candidate biomarker by early detection of lung cancer.
- To analyze and characterize the protein by MALDI-TOF-MS and determine its sequence.
- To study the interrelationship between the expression of candidate marker protein and cancer progression.