Objectives
2. Objectives

Paclitaxel, used either as single agent or in combination with multiple other anti-cancer agents, has been routinely used in adjuvant, non-adjuvant and metastatic setting for a wide range of solid malignancies, including those of breast, prostate, lung, head and neck etc [56,57,59]. However, despite its widespread use, resistance to paclitaxel based chemotherapies has emerged as a global problem, limiting the chemical effectiveness of this important and widely used anti-neoplastic agent [51,102-104,121,156,205-210]. So to combat the problem of paclitaxel resistance it is important to understand the mechanisms leading to paclitaxel resistance. In the previous decade, although substantial amount of research has been expended to understand the mechanisms of intrinsic and acquired paclitaxel resistance, paclitaxel resistance still continued to be global problem. Upregulation of P-glycoprotein (P-gp) and related efflux pumps [207,211] and altered expression of βIII-tubulin isotype and microtubule associated proteins [212-214] has been demonstrated to be the predominant mechanisms for the development of paclitaxel resistance.

However from recent studies it is becoming evident that miRNAs also play important role in the development of paclitaxel resistance. Although they account for less that 1% of all human genes, miRNAs has been claimed to regulate expression of 30% of all protein coding genes [215]. Supporting this, aberrant expression of miRNAs has been observed in various human cancers [216] and has been correlated with tumourgenesis and tumour responsiveness to chemotherapies [122]. To date, an extensive number of studies have identified several miRNAs that have diagnostic, prognostic and therapeutic value for patients with cancer. The functional role of miRNAs in the resistance to microtubule targeting agents (MTAs), however, has only recently begun to be understood. This intrigues us to investigate the role of miRNAs in the development paclitaxel resistance. In this study, we attempted to investigate the role of miRNA differential expression in modulating paclitaxel responsiveness in lung cancer cells and tried to correlate particular miRNA expression with tumor responsiveness to paclitaxel. Previous studies involving NCI-60 panel of cell lines have shown that miRNA expression patterns are better representative of the type and stage in human cancers than classical mRNA profiles [123].
So, this study was undertaken with the following objectives:

- To screen and compare the differential miRNA expression profiles of paclitaxel resistant and sensitive lung cancer cells to identify particular miRNAs responsible for the acquisition of paclitaxel resistant phenotype.

- To identify functional role of candidate miRNA/ miRNAs in the development of paclitaxel based chemo-resistance in NSCLC.

- To elucidate direct relationship between candidate miRNAs with altered expression of survival genes and to correlate particular miRNA expression with tumor responsiveness to paclitaxel.