CONCLUDING REMARKS
There is sufficient evidence that cadmium metal and a number of cadmium compounds, such as cadmium chloride, oxide, sulfate, and sulfide, are carcinogenic in animals. Increased rates of testicular, prostate, and lung cancer in animals have been described. Occupational cohort studies have suggested possible associations between chronic exposure to cadmium and cancers of the lung, prostate, and genitourinary system such as renal carcinoma. The strongest evidence for a linkage between occupational exposure to cadmium and cancer is that of lung cancer. Since cancer is a multi-step process and its occurrence turns on number of cellular signalling mechanisms, existing therapies regarding cancer treatment is somewhat comprehensive, but is not targeted. Chemo and radiotherapies can kill the cancer cells effectively but at the same time it obliterates the normal cells which seem to be an associative cause of immediate death of cancer patients. In this aspect targeted therapies in terms of cancer treatment is an important field of cancer research now a days. The mode of carcinogenesis is different in various organs. So it would be a failure if we try to invent some common drug which is thought to be effective to treat cancer in anywhere in body.

It is important to reveal the internal molecular mechanisms which start playing during carcinogenesis, otherwise we would not be able to develop any effective therapy against cancer. In this regards elucidation of molecular signalling pathway which is activated in lungs of the experimental models, exposed to low concentration of cadmium compound demands significant importance. Peculiarly cadmium shows biphasic dose response relationship which is defined by low dose proliferation and high dose cell death. We observed though very small amount of cadmium may accumulate in mice lung due to systemic circulation while given intraperitonealy, still induced activation of such molecules capable of turning on the cellular signalling
which ultimately leads to cell proliferation. It proves inhalation is not the only cause but ingestion of contaminated foods may promote cadmium induced lung cancer.

The link between chronic inflammation and occurrence of cancer is quite common topic in advance research. We showed that simultaneous activation of proinflammatory cytokines and cell proliferative mediators in lungs exposed in cadmium compound for long duration, both in vivo and in vitro. It is true that application of anti-inflammatory drug only reduced the expression of proinflammatory cytokines, but long term exposure of cadmium compounds, which is more than our experimental periods, would definitely be a cause of inflammation induced lung cancer.

The key regulatory molecule through which cadmium triggers lung cell proliferation is EGFR. Activation of EGFR signalling cascade is quite natural in many cancer. EGFR and other such molecules are essential during developmental process, but regulated by tight molecular information. This controlled synchronisation is destroyed either by mutation or by stimulation of mutagen like cadmium. The uncontrolled expression of growth regulatory molecules is fundamental cause of cancer in adult cell. Cadmium is known to have long half life in animal cell, which in turns increases ROS production and thereby activates EGFR. EGFR can regulate the expression of number of genes producing various cytokines and growth regulatory molecules. Increased expression of cytokines like IL-6, IL-1β, TNF-α and other cell proliferative molecules such as STAT3, Akt, CyclinD1 in cadmium treated lung cell proved the involvement of these mediators cadmium induced lung cancer.

For effective drug designing for a disease like cancer it is important to have a clear conception about the particular signalling pathway which is key player cause the ultimate alteration in the cell. We have shown here that cadmium challenged lung cell
proliferation follows EGFR mediated NF-κβ activation which in turn activates different cytokines and cell proliferative molecules those are very much familiar with onset of cancer. We have clearly emphasized on the fact that inflammation is one of the important feature of heavy metal stimulated cancer mechanism. Though it may be independent sometimes, but severe inflammation is a key factor prior to the cadmium induced carcinogenesis.

To conclude, the present study establishes a new molecular pathway regarding cadmium induced lung cancer in individuals those who are exposed to cadmium contamination either directly or by indirectly. Identification of molecular mechanism of lung cancer caused by cadmium compounds would help to develop specific inhibitors which can turn off the signalling cascade in a target specific manner. The main goal of the preceding study was to investigate the involvement of the molecules. However, this requires further extensive research on the interaction of these participating mediators in more details for a complete conclusion.