SUMMARY
The Indian drug resistant isolates of *Mycobacterium tuberculosis* exhibited a lot of variation in their fingerprints generated on the basis of IS6110 typing. The number of this element in the isolates varied from none to nineteen. At least 60 unique fingerprints were identified.

As there were very few isolates with identical fingerprints it is believed that there are a variety of strains spread within the Indian population. Any single dominant drug resistant strain could not be identified as a causative agent from the samples included in the study.

The drug resistant isolates from Northern India were very different from the ones causing epidemics in the west.

There were a large number of isolates with less than four copies of IS6110. These were better typed using the DR probe.

As large number of Indian isolates do not have requisite copies of IS6110 for developing an unambiguous fingerprint, it is necessary to have better techniques for strain identification. The new method FAFLP was tested as a molecular epidemiology tool. The robustness and superior resolving power of this technique was shown. It offers many advantages over the existing typing techniques.

The primary screening for mutation by SSCP was not foolproof. A lot of false negatives were scored and therefore this technique has to be
carefully used. For this study, sequencing for all the drug target loci was carried out to rule out any ambiguity in the results.

Many known and novel mutations in the drug target loci by automated sequencing were identified. The frequency of these mutations in certain cases was similar to those reported earlier.

The study has established a correlation between certain mutations in rpoB loci and the MIC values exhibited by the rifampicin resistant isolates.

Only two loci for isoniazid resistance namely katG and inhA were investigated. There were many isolates that did not have mutations at these loci but were possibly harbouring mutations in other drug target genes leading to INH resistance. Many novel mutations in the katG loci were identified.

A silent mutation in the rpsL loci in 7 of the streptomycin resistant isolates was characterized. This is a novel mutation however, its contribution to resistance needs to be verified.

A large number of isolates that were resistant to ofloxacin a fluoroquinolone were identified. These drugs form the second line of drugs in TB treatment and are usually prescribed for treating MDR TB. But many of the patients included in this study and had no history of TB treatment had isolates resistant to this drug. This
resistance could have arisen due to poor diagnosis or wrong prescription of drugs.

An important finding of the study was the demonstration of a correlation between the drug resistance and MDR efflux pump in *M. tb*. The data in this study show for the first time that *M. tb.* is capable of developing resistance to drugs by using the drug efflux pumps. One such pump Rv1258c, from a multidrug resistant isolate was characterized in this study.