CHAPTER 5

CONCLUSION & FUTURE WORK

5.1 Conclusion

Current work advances the knowledge of interstitial lung disease, radiological patterns, the predominance of the disease and patterns, disease candidate gene identification, comprehensive enrichment analysis and candidate biomarker discovery. The significant findings of this thesis would expect to improve current diagnostics, prognostics and monitoring procedures in ILDs patients. It could be done by building genetic-based molecular models that would assist in novel therapeutic interventions. Additionally, the effort has been made to develop EHRs system to share and access this information considering security and human rights issues to serve for public health. This research is expected to offer veritable potentials, particularly for the developing countries, including web-based monitoring to provide personalized effective treatments and a better understanding of disease condition.

The first objective of the presented research work was to create an integrated resource for radiological and clinical ILDs presentation. In many developing countries, healthcare services are a system of segregated blocks. Integration of symptoms, pathological and imaging data to provide an efficient diagnosis and treatment is beyond the reach of healthcare systems. Although high-quality health services are available, the majority of the populations cannot afford it. Therefore, efforts should be made to provide better diagnosis through state healthcare services. In this study, EHRs based web-repository was developed to share and access ILDs data. This resource gives due attention to security and human rights issues, and provides anonymized data. Comparative analysis of patterns from different geographical regions offers the opportunity for better understanding of ILDs risks and management. This study also presented a rare lung disease, PAM, with its radiological and clinical pattern analysis, which may update us about the current knowledge of this disease. This web accessible resource for ILDs data (radiological patterns reported in CXRs and HRCTs, relevant patient’s history and lifestyle data) can facilitate computer-aided diagnostics through the development/evaluation of medical image processing algorithms and clinical decision support system (CDSS) which may serve as the second opinion to assist better ILDs monitoring. This study would be valuable to clinicians, especially for radiological training. This web resource, ILD-DB, is expected to work as a uniform resource for public awareness, and it can assist governments and international organizations for framing better policies.
The second objective was to create an integrated genetic knowledgebase of ILDs. ILDgenDB is a unique and centralized knowledgebase that provides diverse genetic data and their analyses related to ILDs. The knowledgebase aims to endow the researchers with a complete and unique platform with unrestricted access to contemporary genetic data and its annotations. This knowledgebase contains 299 literature cured disease candidate genes and their association with biological processes, miRNAs, pathways, and SNPs, etc. The potential role of DCGs in disease pathogenesis is validated using standard resources (GAD, GHR, OMIM, DISEASE, GeneCards, etc.). To incorporate a complete knowledge about ILD pathogenesis, the DCGs involvements in biological processes were identified through gene ontology, pathways and phenotype analyses. The outcomes of downstream analyses of DCGs have revealed the potentially significant role of “molecular binding and inflammatory host defenses”, “immune systems”, and “selective immune processes pathways” in ILDs’ pathogenesis. Several miRNAs, SNPs, and miR-polymorphisms are identified in association studies that account for altered expression of DCGs. The miR-polymorphisms have already verified for their role in cancers, and their role in ILDs can be verified by adopting the similar protocol. Cytokines, interleukins, surfactant proteins, etc., are some of the potential identified DCGs that may have potential involvement in ILDs pathogenesis. These DCGs, pathways, SNPs, etc. can be verified experimentally to serve as diagnostics biomarkers. The main objective of this work is to provide contemporary genetic data in one place to significantly improve the efficacy of ILDs’ management and monitoring through patient-specific therapy and also by providing tools for therapeutic response. Datasets and analysis provided here will be helpful for researchers and scientists working for the betterment of ILDs management.

The third objective was to identify and establish the role of ncRNAs as less-invasive clinical biomarkers of ILDs. The results of this objective have provided the integrated overview of non-coding RNAs, biological pathways and associated genes which are involved in ILDs pathogenesis. This objective has also discussed top regulatory associations. In total, 20 non-coding RNAs and 10 pathways are identified as potential molecular biomarkers and therapeutic targets (Table 1, Table 2, Figure 2). Signaling pathways, inflammatory responses, and cytokine-cytokine receptor interactions are identified as key processes involved in ILDs pathogenesis which could be used as a potential tool for disease diagnostics. Furthermore, this research objective established the association among ncRNAs (IncRNAs & miRNAs), ILDs pathways and immunological processes. These ncRNAs along with pathways could lead us to a novel therapeutic intervention for ILDs. The association between IncRNAs and miRNAs (ceRNAs) is
also established as a potential cause for disease pathogenesis and progression. Non-coding RNAs have already established as a potential tool for disease diagnosis and management. Several ongoing studies have reported that approximately 30-50% of lung biopsies could be prevented by ncRNAs based disease monitoring and management. Sensitivity and specificity of ncRNAs based disease diagnosis is significantly higher than other biomarkers. ncRNAs from body fluid could be used as less-invasive biomarkers for diseases like cancers and ILDs [170]. The outcomes of this research objective are projected to deliver better diagnostics, prognostics, and monitoring of ILDs cases. It would also allow building molecular model using ncRNAs, ILDs-genes, and pathways, which could be used to in new therapeutic interventions.

5.2 Future Work

This research could lead us to explore many possibilities for advancement of radiology and genetics of ILDs. In the future, the two data resources namely ILD-DB and ILDgenDB can be used as a training set and the data can be used for future application development and biomarker discovery. Following enhancement can be incorporated in the existing approach:

- Incorporation of machine learning approaches for supervised classification and identification of ILD’s specific patterns.
- Comparative computer-aided analysis of radiological patterns to differentiate between ILDs and non-ILDs cases, and identify ILDs specific patterns among many ILDs classes.
- Disease candidate genes from ILDgenDB and ncRNAs biomarker can be used as training cases and similar gene expression patterns can be mined for ILDs specific genetic evolution for disease diagnosis and prognosis.