Every individual’s genomic sequences differ considerably and are known as genetic polymorphisms. These variations occur by different types of mechanism like, insertion or deletion of nucleotides, nucleotide substitution, tandem-repeat sequence differences, copy number of genomic segment variations and/or the permutations of any of these changes. A subset of the above said genetic polymorphisms are observed in a population at a frequency of 1% (Nakamura, 2009). The genetic variations are the key biological components underpinning the heritable basis of different phenotypes and evolution. Single nucleotide polymorphisms (SNPs) are the common human genetic variations, which occur approximately at every kilobase (Barnes, 2010). Screening of large number of individuals for these SNPs enables the prediction of susceptibility to a wide range of complex diseases (Jostins et al., 2011). The other types of commonly occurring variations are Copy Number Variations (CNVs). CNVs are structural rearrangements of 1 kb to few mega-bases in size (e.g. duplications, deletions, inversions and translocations). CNVs contribute to human phenotypic diversity and etiology of complex pathologies (Menna, 2014).

Asthma is a respiratory disease, which is characterized by episodes of cough, wheeze and breathlessness and the genetic components contribute with a major frequency to cause asthma. A complex interaction between gene-gene, gene-protein and protein-protein along with the environmental factors play a significant role in causing asthma (van-Eerdewegh et al., 2002; Shapiro., 2002; Ober et al., 2011). Asthma is associated with multiple SNPs of several genes, among them; ADAM33 is one, which is potentially
significant asthma candidate gene. There are many population studies where \textit{ADAM33} was shown to be associated with bronchial hyperresponsiveness and asthma (Kedda et al., 2006; Bijanzadeh et al., 2010).

In view of this, the present investigation was carried to further understand the genetic causes of asthma in South Indian population. The findings and implications of the study are compiled and presented as follows:

\textbf{Section I} reviews what is already known about the asthma, genetic variations and role of \textit{ADAM33} in asthma pathogenesis.

\textbf{Section II} presents the genetic association study of \textit{ADAM33} polymorphisms in asthma. In detail, this section deals with the assessment of clinical phenotypes and severity of asthma, pedigree and patterns of inheritance of asthma and the single nucleotide polymorphisms of \textit{ADAM33} in asthmatics and controls.

\textbf{Section III} deals with the molecular interaction network and pathway analysis of \textit{ADAM33} and copy number variation analysis of asthma related genes.

\textbf{Section IV} summarizes the findings and brings out the future prospects of these investigations.

\textbf{Section V} deals with the literature cited in this thesis

\textbf{Appendices}

1. Chemicals and reagents used

2. Abbreviations

3. List of research publications