Chapter 2

Origin of Hypothesis
Asthma, as discussed, is a complex heterogeneous trait with multiple factors contributing towards its pathogenesis. There are various endo-phenotypes of asthma which are clinically not well diagnosed. Hence identification of these different sub-phenotypes with distinct pathophysiology and clinical outcomes is imperative to tailored therapeutics and clinical management. Finding a model that could predict the occurrence of the disease before the manifestations of actual symptoms is also a need of the hour. Finally if a marker could be identified that would be an indicator of severity and health monitoring, we would be a step ahead in achieving the coveted target of personalized medicine.

Personalized medicine is expected to benefit from combining genomic information with meticulous monitoring of physiological states and metabolome, proteome, transcriptome etc.by multiple high-throughput methods.

As our genome is quite complex, diseases like diabetes, neurological disorders and cancer, likely involves a large number of different genes and biological pathways, as well as environmental contributors that can be difficult to assess. For predictive, diagnostic and treatment of diseases as well as for understanding the onset, development, and occurrence of disease states, the combination of genomic information along with a detailed molecular analysis of samples will be important (Chen et al., Cell., 2012).

With the advancement of technologies it is possible to get resolution of different disciplines in the context of biology with far more details and has augmented our understanding of normal and diseased states.

The cellular and other milieu of the airways in health and disease can be sampled by bronchoalveolar lavage (BAL), bronchial washing (BW), or bronchial biopsies. However these methods are invasive, cause discomfort to volunteer subjects, and are expensive and time consuming, making it difficult to obtain repeated samples. So the use of other lesser and non-invasive matrices such as exhaled breath condensate (EBC), nasal scrapes (NS) which samples the airway lining fluid and nasal respiratory epithelium respectively, can be of great help in identifying biomarkers such as RNA, DNA, lipid mediators, leukotriene and small molecules etc.
With the advances in the high throughput technology large data sets are being generated from different platforms every day. Proteomics (Mass Spectrometry etc.), Metabolomics (Nuclear Magnetic Resonance Spectroscopy etc.), Phenomics (Scoring of clinical parameters), Transcriptomics and several other disciplines seem to add multifarious dimensions into the understanding of complex diseases. Teasing out all these different disciplines ultimately to make some sense would be ideal into unraveling complex pathophysiology. In order to achieve such a holistic viewpoint and knowledge, it is imperative that the multi-dimensional data from multiple ends be threaded and used together, rather than studying them independently.

It is believed; that a complex system involves a close interplay of all this layering of disciplines and it is essential to understand the complex network that exists to generate them. Hence the requirement for integration of all these data using machine learning approaches. Such a systems approach would help us unravel the complexity of asthma and also assist in finding novel sub-phenotypes hitherto unknown. We wish to see how these different clinical and molecular parameters help us in better defining the standards for biomarker discovery for diagnosis and prognosis.