Chapter 4
Central Hypothesis and Objectives
4.1. Central Hypothesis

The central hypothesis to this work is that asthma is too complex to be defined in singular descriptions and functional understanding of asthma will require analysis of multi-variate data including clinical, physiological and molecular profiles. Multidimensional signatures help capture the information that could be missed otherwise. Integration of these informations using a Systems Approach would help address the complexity and assist in the discovery of unknown mechanisms underlying the disease biology. We hypothesize that it might also help discover novel phenotypes. Hence we have taken an integrated approach to address our question of asthma heterogeneity and towards understanding the pathophysiology.

The coming of next generation P4 (Preventive, Predictive, Participatory and Personalized) medicine requires embracing the complexities of the “big data” and discovering differential interactions between health and disease. In childhood asthma, we have approached this problem from a systems viewpoint by integrating clinical assessment, multi-parametric metabolic data, respiratory physiology measurements and state-of-the-art mathematical advancements. The key idea is to build predictive models despite statistical heterodoxies such as highly unbalanced datasets and presence of sub-classes (endo-phenotypes) within a main class. We demonstrate the caution and the pay-offs with integrating such computation-intensive models with clinical data for tailored therapy.

4.2. Aims and Objectives

The aim of this study is to delineate asthma pathophysiology using multi-dimensional ‘omics approach. To achieve that, the following two objectives were undertaken:

C. To differentiate between normals and asthmatics and to identify different sub-phenotypes of asthma based on omics approach:
   - **Metabolomics**
   - **Proteomics**
   - **Transcriptomics**

D. To investigate genetic differences and/or other factors that may contribute towards asthma pathogenesis.