Chapter 1

Introduction
Asthma is a chronic inflammatory condition affecting the airways leading to airway hyper-responsiveness and reversible episodic obstruction. Pathologic features include bronchoconstriction, mucus metaplasia and increased inflammation; commonly related to allergen exposure. Asthma is a major cause of chronic morbidity and mortality throughout the world and there is evidence that it has increased in the last decade, especially in children (GINA). It is a complex disorder and a plethora of genetic and environmental factors contribute to its pathogenesis. At a finer level of understanding that encompasses metabolomic, transcriptomic, proteomic, phenomic, and environmental components, asthma is a heterogenous disorder. Hence, to better understand the pathogenesis of asthma, it is important that asthma be investigated using multidimensional approaches. A broad-based ‘omics’ investigation which encompasses multiple complementary systems namely metabolomics, transcriptomics, phenomics, genomics, miRNomics etc. in a highly phenotyped prospective asthma cohort, is one possibility.

Figure 1: Overview of a systems biology approach to lung disease, with emphasis on the different scales of investigation. Starting with the whole person (A), lung disease can be understood through clinical symptoms as well as various tools such as imaging (B), physiology (C), and analysis of exhaled breath (D). At the whole organ level (E), the lung can be examined at the level of tissues (F), cells (G), and cellular and molecular components (H). The lung can finally be analyzed at the level of gene arrays (I) and the DNA itself (J). Ultimately, the entire process relates back to the human condition (A), but only if the data sets from each of the different scales are integrated (Kaminsky et al, J Appl Physiol., 2010).
A systems approach to understand the complexity of biological phenomenon has many advantages over looking at them in isolation. Integration of metabolite profiling with other multiple ‘omics’ data stitched together, using bioinformatics (Machine Learning), is essential to reconstruct complex networks that characterize phenotypes in the disease biology (Fukushima et al, Curr Opin Chem Biol., 2009).

Respiratory diseases are remarkably complex due to the intricate physiology and biochemistry of the lung, whose range of function varies from the molecular (e.g., gas exchange) to the whole organ level (e.g., bulk flow of air) and involves a myriad of intermediates including the DNA, RNA, proteins, metabolites, etc. An understanding of respiratory health and disease must therefore necessarily encompass information from across this broad scale of organ structure and function. This information could be gathered from integrative physiology and molecular biology and is currently best obtained by a quantitative systems biology approach.