Final Report
National Heart, Lung, and Blood Institute
Level 1 Strategic Planning Working Group
June 27-28, 2006

Lung Program – Theme # 4: Personalized Medicine

Introduction:

The fundamental concept of "Personalized Medicine" is that all individuals have unique characteristics, defined by their genome, and that human variability in health and disease, and individual response to treatment, is based on the individual's genetic makeup in response to their unique environmental exposures. Because it directly interacts with the environment, the lung is a prime example of this concept, with each individual's genome dictating variations in lung function and response to the stress of inhaled substances.

After surveying the current understanding of the definitions, pathogenesis, diagnosis and therapies of the major lung disorders, and the state of knowledge of how genomic variability influences the lung phenotype in health and disease, the Working Group concluded that pulmonary medicine is on the cusp of major advancements in redefining lung diseases on a genetic level, integrating genetic and molecular ("-omics") phenotypes to understand the pathogenesis of lung disease, identifying targets for therapeutic intervention, and defining biomarkers/surrogates that represent the lung in health and disease.

Vision: Genetic and environmental variables determine an individual's disease risk, disease manifestations, and treatment response. Our vision is to initiate in an ethically informed and appropriate manner a nationwide lung genome project that will lead to the understanding of the genetic and environmental basis of lung disease, and enable physicians to individually tailor diagnosis, prognosis, treatment, and prevention strategies for patients with lung diseases based upon individual genotypic and phenotypic characteristics. Based on this vision, the Working Group believes historic advances in combating lung disease can be made if the following recommendations are carried out:

Recommendations:

1. Establish a lung genome project, a nationwide, multi-disciplinary, multi-institutional project that will define the genetic basis of lung function in health and disease. Using state-of-the-art genomics, imaging and "-omics" phenotyping technologies, including characterization of environmental stresses impacting the lung, and including representative groups of the US population:

- Identify the genetic variations that determine variability of lung function in health in the general population, from development through senescence;

- Determine the genetic basis of susceptibility and resistance to the major lung diseases, using the data to develop strategies to predict, prevent and treat lung disease for the individual; and
- Define genetic variations that determine individual responses to the environment, and determine how different environmental stresses modify normal lung development, growth and senescence, and cause and/or modulate the major lung disorders.

2. Combine state-of-the-art lung-related genomic and phenotyping technologies to redefine the major categories of lung disease for personalized medicine. The current categories of lung disease, based on classic physiologic, imaging and histologic criteria, mask conceptualization of disease pathogenesis on a molecular level. With the information acquired in the lung genome project, it will be possible to:

- Redefine lung disorders on a genetic and "–omic" molecular basis, permitting re-categorization of the classic lung disorders into subcategories relevant to the individual; and
- With full attention to issues of patient confidentiality and other possible research risks, carry out longitudinal studies of representative populations to establish natural history and responses to current therapies based on the genetic and "-omic" reclassification of lung disease.

3. Establish new, verifiable markers and surrogates of lung disease. The ability to screen for early lung disease, to follow the course of lung disease over time, and identify the responses of lung disease to therapy will be greatly aided by establishing easily obtained, sensitive markers and surrogates of the disease process. Specifically:

- Develop and validate markers and surrogates of lung function in health and disease using state-of-the-art genetic, molecular phenotype and imaging technologies; and
- Use this information to identify treatment options tailored to the individual, predict disease outcomes, and identify at-risk individuals to initiate preventive strategies.

4. Develop new classes of drugs to prevent and treat lung disease on a personalized basis. While lung disease is a major cause of morbidity and mortality worldwide, other than for asthma, we have no specific, effective therapies for most lung disorders. Redefining lung disorders on a genetic and "-omic" molecular basis, and identifying verifiable markers and surrogates of lung disease will set the stage for a major effort to target therapies for initiation of a major effort to target therapies at the cause of lung disease of the individual in the context of the environment to which they are exposed. Successful development of new classes of effective therapies for lung disease can only be accomplished by innovative NIH - pharmaceutical industry partnerships.

- Launch a major initiative in partnership with the pharmaceutical industry to develop new classes of drugs to prevent and treat lung disease.

5. Develop new paradigms of multi-disciplinary, multi-institutional collaborative programs to study lung disease. While it is critical to preserve the traditional work of individual investigators, the lung genome project will require changing the paradigm of how traditional science is done, shifting the emphasis toward multi-disciplinary, multi-institutional collaborative studies. In this collaborative paradigm:

- Develop standard and shareable database formats for genetic and phenotyping information, establishing for investigators of all disciplines the genetic basis of lung function in the overall population in health and disease; and
- Develop relevant clinical and statistical tools to test the impact of identified variants on treatment responses; use the information to direct Lung Personalized Medicine.

6. Establish a cohort of personalized medicine investigators in lung disease. To successfully accomplish the lung genome project, it will be critical to:

- Develop and fund mechanisms for education in bioinformatics, genetics, and genomics among entry level trainees, junior level investigators, minority investigators, and established investigators;
- Develop a personalized medicine scholars program and ethics training opportunities relative to personalized medicine;
- Establish time-limited intensive training opportunities in personalized medicine; and
- Mandate personalized medicine training within established training mechanisms, and in personalized medicine components to SCCOR and funded network grant mechanisms.

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