Complementing the Genome with the Exposome: Mapping Environmental Exposures

Complex diseases are known to have both genetic and environmental components. Low-level and prevalent environmental exposures may contribute substantially to the burden of common complex disease (Hemminki et al, 2006, Gibson, 2008). Characterization of susceptibility is rapidly advancing through application of microarray technology for genotyping and investment in large genome-wide association (GWA) studies (McCarthy et al, 2008). Epidemiologists are now facing the challenges associated with interpreting this massive amount of genomic variation data for understanding etiology of complex environmental disease. Calls for tools to characterize and unravel interacting genetic and environmental factors have begun (Collins, 2006; Manolio and Collins, 2007).

Despite these calls, accurate assessment of environmental exposures remains an outstanding and largely unmet challenge; characterization of exposure remains primitive and resources to improve the scientific basis of exposure assessment are limited or nonexistent. This raises the question as to whether fundamental knowledge about genetics will improve understanding of disease etiology at the population level (Wild, 2005). One side of the gene-environment equation continues to be refined while the other remains subject to crude characterization. Due to the complex nature of the human system, predictions of potential health risks associated with environmental exposures will be limited by the least resolved or least understood component of the system. By focusing resources exclusively on characterizing genetic susceptibility we compromise the ability to fully realize benefits of the genome and of large GWA (genome wide association) studies. Just as a new generation of scientific tools has provided the ability to efficiently assess genetic susceptibility, there is a critical need to develop methods for characterizing environmental exposures at biologically-relevant resolution.

Understanding the contribution of environmental factors to disease susceptibility will require a more comprehensive view of exposure and biological response than has traditionally been applied. Wild (2005) has proposed the need for a "step change" in exposure assessment and has articulated a vision for exposure measurement calling for an "exposome," or measurement of the life-course of environmental exposures to provide the evidence base for public health decisions to address environmental health. Wild and others (e.g., Wild 2009) discuss the potential of emerging technologies to provide this new generation of exposure information. In their guest editorial in EHP, Smith and Rappaport (2009) argue that if we expect to have any success at identifying the contribution of environmental factors on chronic diseases, we must develop 21st-century tools to measure exposure levels in human populations and to quantify the exposome.

This past February, the National Academies of Science organized a workshop titled "The Exposome: A Powerful Approach for Evaluating Environmental Exposures and Their Influences on Human Disease" to examine the concept of the exposome and its importance to the etiology of human diseases. A strategy for utilizing banked samples from large birth cohort studies to develop, evaluate and pilot advanced biomarkers to map the Exposome was presented.

Mapping the Exposome is a grand scientific challenge of national and international importance. The Exposome is required to measure exposure and to elucidate the impact of environment on biology and on disease. Without investment in advanced technology to measure and diagnose exposures, the potential of our national investment in the genome, in genetic epidemiology and in personalized medicine cannot be realized.

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