The MURDOCK Study: A Framingham for the Genomic Era

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Abstract

The study and characterization of disease has traditionally been based upon crude characterization of clinical characteristics, radiographs, and laboratory tests developed over the past several decades. Centered in Kannapolis, NC, the M.U.R.D.O.C.K. Study (Measurement to Understand Reclassification of Disease Of Cabarrrus/Kannapolis) is a long-term epidemiological study that aims to segment diseases by combining best-in-class clinical research, statistical, and analytical methods with different omics technologies and electronic health records. In doing so, we will be able to reclassify health and disease based on underlying causal factors, thus helping to realize the vision of personalized medicine—the right treatment for the right patient, at the right time. In this talk I will present the MURDOCK Study, with an emphasis on the MURDOCK Integrated Data Repository (MIDR) both as an informatics challenge and a resource for analysis and collaboration.

Introduction and Background:

A confluence of high throughput “omic” technologies, along with increasing adoption of electronic health records, has enabled a new paradigm for biomedical research and discovery. Instead of collecting phenotypic data at a macroscopic level, we can now measure thousands of variables in the form of molecular signatures, as well as perform data mining on a large and rich corpus of clinical data collected in the course of care. These additional sources of data enable the reclassification of disease using molecular biomarkers of physiological dysfunction. This in turn enables us to facilitate development of therapeutic interventions as well as disease prevention strategies. The MURDOCK Study is a long-term epidemiological study that applies this new research paradigm to major chronic illnesses, helping to improve disease classification and population health.

Methods:
The MURDOCK study consists of distinct project “horizons” or stages. Horizon 1 involves the generation and analysis of molecular data for existing large, clinically well-annotated cohorts of four different diseases: Cardiovascular disease, Osteoarthritis, Obesity, and Hepatitis C. Biological assays including genetic, genomic, proteomic, metabolomic, and imaging techniques have been performed across these different cohorts. Statistical methods such as Sparse Bayesian Factor Analysis and Principle Components Analysis have been applied to these datasets to identify biomarker signatures predictive of disease outcomes, e.g. disease progression and response to therapy. Horizon 1.5 involves the creation and population of a 50,000 volunteer registry for Horizon 1 validation and prospective studies. Blood and urine are collected, along with clinical data through a questionnaire, permission to access electronic health records, and permission to re-contact the subject to participate in future studies. Horizon 2 projects leverage and prospectively recruit the volunteers enrolled in Horizon 1.5, and extend the study to additional disease areas of interest, for example multiple sclerosis, aging, and cognitive impairment.

Results:
Clinical data collected through the case report forms for the four individual Horizon 1 studies have been mapped to common data elements, where such overlap exists. Preliminary molecular and imaging data analysis has yielded promising biomarkers such as a proteomic signature for response to interferon therapy in Hepatitis C [1]. Development of the MURDOCK Integrated Data Repository (MIDR) is ongoing to bring together clinical and molecular data, as well as sample and study metadata for the remainder of the Horizons.

Discussion:
The MURDOCK study represents a new model of translational investigation, a whole much greater than the sum of its parts, and a prime example of what can be achieved through team science. As biological assays improve and expand, and as well-defined standards are agreed upon for common data elements, new approaches to biomedical research become feasible where they would have been impossible only a decade ago. The MURDOCK Study is actively seeking collaborators for novel approaches to analysis of the rich resources that the MIDR and MURDOCK biospecimens represent.