Coriell Personalized Medicine Collaborative

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New Jersey’s Coriell Institute in Vanguard of Personalized Medicine Initiatives

At present, medicine is generally practiced using a one-size-fits-all approach which tragically results in 2 million serious adverse drug reactions annually and 137,000 deaths — accounting for six percent of hospitalizations in the United States and billions of dollars in healthcare costs. In the setting of personalized medicine, however, a medical professional can consult a patient’s personal genetic profile to determine which drugs will be most effective and which are likely to result in toxic side effects, as well as the diseases for which a patient is at elevated risk.

Personalized medicine, also referred to as genome-informed medicine, will soon become a reality, but many issues remain regarding its implementation. Enter the Coriell Personalized Medicine Collaborative, a research study led by the Camden, NJ-based Coriell Institute for Medical Research.

The Coriell Personalized Medicine Collaborative (CPMC) is a research study that employs an evidence-based approach to determine the utility of using personal genome information in health management and clinical decision-making. The CPMC also aims to discover genetic variants that affect drug toxicity and efficacy, as well as to identify presently unknown gene variants that elevate a person’s risk of cancer and other complex diseases.

Promises of Personalized Medicine and Challenges of Implementation

Genome-informed medicine is the use of an individual’s genetic information to predict disease, avoid adverse drug reactions and tailor treatment. This form of medicine has the potential to lower healthcare costs in a number of ways, such as increasing preventative care or “prospective medicine” in focused populations; increasing the effectiveness of treating individuals by greatly reducing the trial-and-error associated with prescribing many medications, such as anti-depressants and painkillers; and by lowering the number of adverse events through genetically tailored treatments. However, there are challenges to the successful implementation of personalized medicine, including the potential for personal genetic information to be misinterpreted by healthcare professionals, leading to unnecessary medical tests, or misunderstood by individuals, leading to disillusionment, anxiety and confusion. There is also the potential that this information could be used unscrupulously, leading to genetic discrimination.

Factors contributing to the slow integration of personalized medicine into medical care include the development of decision support algorithms that utilize genomic data, a lack of genetic and genomic education for healthcare providers, and the absence of evidence-based research that establishes the clear benefit of personalized medicine. While data exist to support the associations between genetic variants and disease, there is a paucity of data establishing that genetic data have a clear health benefit.

The successful implementation of personalized medicine is dependent upon several factors, including a critical need to educate health professionals. The amount of genetics traditionally taught in medical schools is limited and typically focused on single-gene disorders and chromosome abnormalities, with little exposure of students to complex genetics. Additionally, the implementation of personalized medicine requires government support and regulatory oversight, as well as public vetting of ethical issues. Finally, medical records systems must be structured to accept genetic data and integrate them with the patient’s existing health record in a way that facilitates use in clinical decision-making. Another obstacle for evidence-based research into the effectiveness of personalized medicine is the need for large cohorts and longitudinal data collection to generate sufficient data to compute the treatment effect and gauge the potential costs and benefits.

Need for Evidence-Based Research Studies

With the completion of the Human Genome Project, the more recent understanding of patterns of human genetic variation through the SNP Consortium and the HapMap Project, and dramatic advances in the technology required to profile genomes, the time to implement personalized medicine is now. To understand the utility of genome information in healthcare, the mechanism for sharing genetic variation information associated with complex diseases with individuals and healthcare providers must be constructed, and evidence-based studies must be performed to assess the outcomes from the receipt and utilization of this information. These are the major goals of Coriell’s research study.
The Coriell Approach

The Coriell Personalized Medicine Collaborative (CPMC) aims to be a model for the ethical, legal and responsible implementation of genome-informed personalized medicine. This forward-looking, collaborative effort involves physicians, scientists, ethicists, genetic counselors, information technology experts and volunteer study participants and will enroll 10,000 individuals by the end of 2009, with an ultimate goal of 100,000 participants. As of December 2008, there were 3,300 participants enrolled in the study.

An outline of the CPMC research study is shown below in Figure 1. Currently, individuals interested in participating in the research study must attend an informed consent session to learn about the study and enrollment process, read and sign a consent form, and submit a small saliva sample. Eligibility requirements to participate in the CPMC include being eighteen years or older and having a valid email address. Participants must also be willing to complete web-based surveys during the course of several years to assess health and behavioral outcomes related to the personal genetic variant information released by the study.

Figure 1. Outline of the CPMC Research Study

The CPMC research study involves (1) informed consent and saliva collection; (2) genotyping; (3) genetic results; (4) optional sharing of genetic results; and (5) outcomes research.

To identify sites of genetic variation, DNA is isolated from study participants’ saliva samples and processed in Coriell’s Genotyping and Microarray Center—a Clinical Laboratory Improvement Act (CLIA)-approved, multi-million dollar facility. The CPMC utilizes an outside advisory board termed the "Informed Cohort Oversight Board" (ICOB) to determine which genetic information is deemed "potentially medically actionable" and, therefore, returned to study participants.

When the CPMC web portal launches in early 2009, study participants will register personal CPMC accounts through the secure online portal and complete online medical history, family history and lifestyle questionnaires. These data will be used in combination with personal genome information to calculate personalized risk. Study participants will have the option to view "potentially medically actionable" information about their genomic profiles: sites in their DNA that are associated with diseases for which there is some treatment or intervention that may be able to reduce the risk for those diseases.

Participants have the option to share some or all of their genetic results with their physician(s) and may also discuss their results with a board-certified CPMC genetic counselor at no cost. A variety of educational materials on genomics and medicine will be provided through streaming video and downloads on the web portal. Additionally, educational seminars will be hosted by CPMC genetic counselors and hospital partner physicians and will focus on the conditions reported by the CPMC study.

Follow-up studies of the actions of CPMC participants and healthcare providers, as well as participant health outcomes, are at the heart of this evidence-based study. A variety of outcome measures are assessed via web-based surveys completed by participants regarding their actions, physician actions, attitudes and, ultimately, health outcomes.

Currently, the CPMC is funded through private philanthropy, foundation grants and institutional support, with no cost to individual study participants.

Regulating the CPMC: The Informed Cohort Oversight Board

The purpose of the ICOB is to evaluate the medical "actionability" of health conditions to determine what personal genetic variant information will be returned to study participants. Factors to be considered include recommendations by organizations such as the US Food and Drug Administration and the Centers for Disease Control and Prevention, as well as the number, size and quality of studies demonstrating statistically significant association of a gene variant with the condition. The ICOB simply approves what genetic information is available to participants—it is then an individual’s choice whether or not to view their status at these sites.

This external advisory board comprises highly esteemed scientists, healthcare professionals, an ethicist and a community pastor. The ICOB meets at least twice per year, a frequency which allows Coriell to continuously update the list of genetic results reported by the CPMC. The decisions of the
ICOB, and their reasoning, will be made publicly available through the CPMC web portal.

Engagement of Hospital Partners and Medical Professionals

With respect to the challenge of integrating genomic information into routine medical care, educating medical professionals, particularly doctors and nurses, is likely to be a rate-limiting step. Coriell understands the importance of engaging clinicians and other medical professionals to develop successful strategies for integrating complex genetic information into the current medical paradigm and does so by bringing these individuals into the CPMC both as collaborators and participants. In addition, Coriell appreciates the commonality of cancer in society and the enormous potential for cancer research and cancer care to be impacted by personalized medicine. Thus, Coriell has established collaborations with neighboring healthcare partners for the CPMC study.

Coriell established a partnership with next-door neighbor and tertiary teaching hospital, Cooper University Hospital, in March 2008. Cooper University Hospital is the clinical campus for the Robert Wood Johnson Medical School of the University of Medicine and Dentistry of New Jersey and has more than 550 physicians in more than seventy-five subspecialties. In July 2008, Coriell announced its collaboration with community-based Virtua Health — a collaboration stemming from the understanding that most of the population is treated in community health centers, as opposed to academic medical centers, which are often located in urban areas. Virtua is a community health system with four hospitals, numerous outpatient centers and more than 1,800 physicians in its network. Coriell also formed a collaborative relationship with Fox Chase Cancer Center, one of thirty-nine National Cancer Institute-designated comprehensive cancer centers with a long tradition of excellence in combining state-of-the-art patient care with cutting-edge genetic research. In addition, a number of other partnerships with the CPMC are being discussed. Coriell encourages the enrollment of medical professionals and health center employees into the research study, as these ties energize the study and open the door to educate medical professionals about genomics.

Coriell is also looking to medical professionals for input to ensure that effective mechanisms are developed for using genomic data in the clinical setting. Questions to be addressed include how genome information is best conveyed in the typical twelve-minute office visit, and what resources and tools are needed by healthcare providers to appropriately use genome information and educate their patients.

Realization of genomic medicine will require a two-way exchange in which scientists educate medical professionals and vice versa. Coriell expects that the deep engagement of several hospital partners in the CPMC will spark this dialogue. Moreover, it is anticipated that as CPMC participants invite their healthcare providers to view their personal genomic results, Coriell will have an engaged and accessible population of healthcare providers to whom targeted surveys may be directed regarding use of genome information in medical care.

Researchers in the Genotyping and Microarray Center process DNA samples to determine individual genome profiles. Pictured are Norman Weiner and Lori Swanson of the Coriell Institute.

CPMC's Cancer Arm

Coriell’s partnership with healthcare centers including Fox Chase Cancer Center enables the study to have a cancer arm in addition to the wellness arm described previously. Among the first 10,000 study participants, the goal is to enroll 2,500 patients with breast cancer and 2,500 patients with prostate cancer. There is evidence that the baseline risk to develop cancer is strongly influenced by genetic variation and that in cancer patients, the response to chemotherapeutic agents, adverse events from medication and clinical outcomes are influenced by a patient’s genetic makeup. The creation of a large breast and prostate cancer population will allow researchers to examine the role of genetic variants in pharmacogenomic and clinical endpoints.

Participant Privacy and Security

Coriell has a number of mechanisms designed to maintain the integrity, confidentiality and security of its data and information systems. Security policies are in place to assure that all data are protected from unauthorized access, and Coriell maintains audit trails, backup procedures and error checking continued on page 10
to assure accuracy and protection of CPMC data. Personally identifying information is encrypted and stored in a database separate from the genotype and medical data.

Outreach to Minority Populations

As the population of participant volunteers in the CPMC grows, Coriell is dedicated to ensuring that the genetic data collected are representative of the ethnic composition of the region. The community in which the Coriell Institute is located, Camden, NJ, is one of the poorest urban communities in the country, primarily made up of African-American and Hispanic residents. Coriell’s aim is to develop mechanisms to reach these historically underserved communities.

Coriell has enlisted the support of several groups to aid in minority recruitment. First, Coriell approached the religious community in Camden County, NJ. Additionally, prominent leaders are taking part in the study and offering assistance in reaching minority populations. Within the Hispanic and Latino community, Coriell has engaged local Hispanic political leaders including United States Senator Robert Menendez (D-NJ), co-sponsor of S.976, “Genomics and Personalized Medicine Act of 2007.”

Coriell Institute and the CPMC

The CPMC, an evidence-based research study designed to determine which elements of personal genetic data are valuable in clinical decision-making and healthcare outcomes, was spearheaded by Coriell’s President and CEO, Michael F. Christman, Ph.D., and puts the Institute at the forefront of this revolution in medical care.

The Coriell Institute was founded in 1953 and is the world’s leading biobank — distributing biomaterials to researchers throughout the world for the study of human diseases and aging. To learn more about Coriell and the Coriell Personalized Medicine Collaborative, visit www.coriell.org.

References

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