



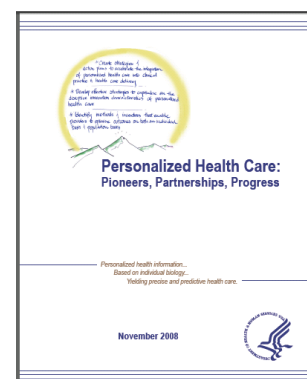
# The Coriell Personalized Medicine Collaborative

## *Examining the Utility of Genome-Informed Medicine*

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### **Executive Summary**

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 build a cohort with rich genotypic and phenotypic data with which to discover genetic variants that affect drug toxicity and efficacy, as well as to discover presently unknown gene variants that elevate a person's risk of cancer and other complex diseases.

This forward-looking, collaborative effort involves physicians, scientists, ethicists, genetic counselors, volunteer study participants, and information technology experts. Its goal is to better understand the impact of personalized, or genome-informed, medicine and guide its ethical, legal and responsible implementation. The study will enroll 10,000 individuals by the end of 2009 with an ultimate goal of 100,000 participants. As of October 2008, there were 3,000 participants enrolled in the study. There is no charge to study participants.

### **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<sup>1-3</sup>. This form of medicine has the potential to lower healthcare costs by 1) increasing preventative care or "prospective medicine"<sup>4-6</sup> in focused populations; 2) increasing the effectiveness of treating individuals by greatly reducing the trial-and-error associated with prescribing many medications, such as anti-depressants and analgesia; and 3) lowering the number of adverse events through genetically tailored treatments. This is best exemplified in the field of cardiology, where personalized medicine has changed the standards for prescribing beta-blockers<sup>7</sup> and ACE inhibitors<sup>8</sup>. However, there are challenges to successful implementation of personalized medicine<sup>9-11</sup>. There is the potential for personal genetic information to be 1) misinterpreted by healthcare professionals, leading to unnecessary medical tests; 2) misunderstood by individuals, leading to disillusionment, anxiety and confusion; and 3) used unscrupulously, leading to genetic discrimination.

Factors contributing to the slow integration of personalized medicine into medical care include 1) the development of decision support algorithms that utilize genomic data such as those under development for implementation of variant-specific dosing, as is the case of pharmacogenomic variants such as those that affect warfarin dosing<sup>12</sup>; 2) a lack of genetic and genomic education for healthcare providers; and 3) 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<sup>13-16</sup>. 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<sup>17-19</sup>, as well as public vetting of ethical issues<sup>20, 21</sup>. 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. Cohort size must be large enough to address 1) genetic variants of low frequency (~1 to 2 percent), 2) gene-environment effects, 3) gene-gene interactions, and 4) loss of participants to follow-up. There are also consent and privacy issues that come into play in large cohort studies<sup>22</sup>. In addition, genetic studies of large cohorts require significant biobanking, genotyping and information technology infrastructure<sup>23</sup>.

### **The Importance of Biobanking**

The mission of the Coriell Institute includes the collection, characterization, storage, and distribution of valuable biomaterials and associated data for scientific research. Coriell has more than forty years experience in developing and maintaining biorepositories as national and international resources for the study of human diseases and aging. The Institute continues to expand its information management systems to meet evolving business and scientific requirements. Coriell has a state-of-the-art laboratory and data management system and a web-based catalog for biomaterials and associated data.

Since the inception of the Coriell Cell Repositories, more than 150,000 cell cultures have been distributed to investigators in laboratories in the United States and sixty-two foreign countries. More than 500,000 aliquots of DNA have been shipped from all Coriell-managed repositories to investigators throughout the world. Coriell's Repository Information Management System was designed to facilitate and streamline high-volume biomaterials and data distribution management. Coriell has been managing web-based access to genome-wide genotype data on hundreds of samples in its collections during the past several years. Its biorepository capabilities include significant phenotypic data management, with use of standardized phenotypic language and collection of longitudinal data for its disease collections<sup>24, 25</sup>. Additionally, Coriell has partnered with several regional healthcare systems that are rapidly moving toward comprehensive electronic medical record systems. These assets position Coriell and its partners to meet the challenges of translating genomics into clinical practice.

### **Need for Evidence-Based Research Studies**

The Human Genome Project<sup>26</sup> and the more recent understanding of patterns of human genetic variation through the SNP Consortium<sup>27</sup> and the HapMap Project<sup>28</sup> have served to lay the foundation for the next generation of efforts to map complex disease genes and the quantitative trait loci (QTLs)<sup>29</sup> that may be preclinical indicators of pending disease. To make this information useful in improving health and the quality of life, 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 receipt and utilization of this information. These are the major goals of Coriell's research study.

The importance and need for an evidence-based initiative has not gone unrecognized by others in the scientific community. Dr. Francis Collins, former National Human Genome Research Institute director and human genome project pioneer, stated in a June 6, 2008, interview with Science magazine, "We desperately need, in this country, a large-scale, prospective, population-based cohort study. And we need to enroll at a minimum half a million people. We would need to have their environmental exposures carefully monitored and recorded, their DNA information recorded, their electronic medical records included, and have them consented for all sorts of other follow-ups." The cost to perform such a study has been estimated at 300 to 400 million dollars per year. Coriell's CPMC study has been constructed such that participants may opt to share their anonymized genotypic and phenotypic data with the scientific community, where it can be combined with other datasets in large genome-wide association studies.

### **The Coriell Approach**

The CPMC aims to be a model for the ethical, legal and responsible implementation of genome-informed personalized medicine. The CPMC study is structured to allow dynamic communications between Coriell and study participants using a secure web portal. Web-based surveys will be used to assess health and behavioral outcomes related to the personal genetic variant information released by the study. Additionally, this portal will allow participants to share their data with healthcare professionals. Currently, the CPMC is funded through private philanthropy, foundation grants and some institutional support, with no cost to individual study participants. An outline of the CPMC research study is shown below (Figure 1).

After participants have given their informed consent, they are asked to donate two milliliters of saliva for genome profiling using a microarray platform (Affymetrix 6.0 Genechip, Affymetrix, Santa Clara, CA) and targeted SNP profiling using a bead-based platform (Illumina BeadXpress, Illumina, San Diego, CA). An outside panel termed the "Informed Cohort Oversight Board" (ICOB) meets at least twice per year to review genetic variants submitted by Coriell as risk variants for health conditions. Only genetic variants associated with health conditions considered to be potentially medically actionable (i.e., where there is the potential to mitigate risk, and those variants for which a significant association has been replicated) are then returned to participants via a secure web portal. Participants are able to grant access to their physician(s) to view the results and may request to discuss their results with a CPMC

genetic counselor at no cost. A variety of outcome measures are assessed via web-based surveys completed by participants regarding their actions, physician actions, attitudes and, ultimately, health outcomes. Participants are asked to update their medical, family and lifestyle information annually such that longitudinal datasets are generated. Thus, there are several dynamic aspects of the CPMC, including ongoing review of association studies to identify variants for submission to the ICOB, continual outcomes research and the longitudinal collection of participant medical records on an annual basis.



**Figure 1.** Outline of the CPMC Research Study

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

**Engagement of Hospital Partners and Medical Professionals**

With respect to the challenge of integrating genomic information into routine medical care, the education of 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 engaging these individuals in 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. The collaboration with Virtua was born out of 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. These ties energize the study and open the door to educate medical professionals about genomics.

One of the strategies to educate medical professionals will involve seminars given by Coriell scientists, CPMC genetic counselors and hospital partner physicians. Currently, Coriell is developing a seminar series on genomic medicine in collaboration with partner hospitals. Seminars will focus on diseases included in the CPMC and will meet the requirements of Continuing Medical Education (CME) such that attendees may gain CME credits. In an attempt to make education as accessible to healthcare providers as possible, Coriell may also post the genomic medicine seminars online as webcasts.

Coriell will also look to medical professionals for input to ensure effective mechanisms are developed for using genomic data in the clinical setting. Questions to be addressed include:

- How is genome information best conveyed in the typical twelve-minute office visit?
- What type of information do healthcare providers want to see in a genome-wide genetic test report and in what context?
- 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. This exchange will involve traditional communication in addition to that of medical and genetic datasets (in the form of

electronic medical records and large numbers of genetic test results, respectively). Coriell expects that the deep engagement of several hospital partners in the CPMC will catalyze this dialogue. Moreover, it is anticipated that as CPMC participants invite their healthcare providers to view their personal genetic 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.

### **Recruitment of CPMC Study Participants**

Recruitment of individuals into the CPMC is primarily conducted during informed consent sessions held at the Coriell Institute, partner hospitals or other community locations. The principal investigator of the CPMC, or a CPMC scientist, discusses the details of the study, possible risks, the content of the Informed Consent document, and provides attendees with the opportunity to ask questions. Upon signing of the Informed Consent document, newly enrolled individuals are invited to submit a small saliva sample. There is no charge to participants in the CPMC study.

Eligibility requirements are limited to requiring that participants are eighteen years old and older, have a valid email address and are willing to complete web-based surveys during the course of several years. Participants may opt (at the time of enrollment or any time thereafter via the secure web portal) to release their anonymized genome-wide variant data and medical history data to the scientific community for association studies.

### **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 above. Among the first 10,000 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. Thus, the creation of a large cohort of breast and prostate cancer patients with rich phenotypic datasets from the national cancer registries, as well as genome-wide genetic information, will allow researchers to examine the role of genetic variants in pharmacogenomic and clinical endpoints. For those participants who agree to allow the CPMC to share their anonymized data, such data will be made available to the larger scientific community through the National Center for Biotechnology Information (NCBI) database of Genotype and Phenotype (dbGaP) resource.

### **Clinical Laboratory Improvement Act (CLIA) Compliance**

The CPMC's goal to examine the potential use of genome information in clinical practice requires that the testing be performed in a Clinical Laboratory Improvement Act (CLIA)-approved laboratory. Therefore, the Coriell Genotyping and Microarray Center applied for and obtained CLIA certification to perform genotyping assays using the Affymetrix GeneChip platform. Soon, Coriell will expand its initial application to include CLIA certification for genotyping using the Illumina BeadExpress platform.

### **Powerful Analysis: Coriell Genotyping and Microarray Center**

The Coriell Genotyping and Microarray Center uses the Affymetrix Genome-Wide Human SNP Array 6.0. The Affymetrix array was designed to provide broad coverage of SNPs across the entire genome through genotyping at more than 900,000 SNPs. Due to this design, SNPs known to have an association with a particular phenotype may not be present on the chip or represented through a perfect proxy SNP. To compensate, Coriell will use custom-designed SNP panels to include the disease-relevant SNPs absent from the Affymetrix platform. These panels will be analyzed on the Illumina BeadExpress platform.

### **Regulatory Body: Informed Cohort Oversight Board**

The purpose of the Informed Cohort Oversight Board (ICOB) is to evaluate the medical actionability of health conditions and the evidence of a genetic risk variant's potential medical "actionability" with regard to this health condition. A major prerequisite for consideration of genetic variants is the validity of association studies in the published literature that suggest a significant association between genetic variants and specific medical conditions. The ICOB thereby determines what personal genetic variant information will be returned to study participants. Approval is given when knowledge of a participant's status for a particular genetic variant has the potential to affect a healthcare provider's treatment course or permit the provider to offer advice about the participant's health or lifestyle that has the potential to mitigate risk. Using prospective, web-based outcomes surveys, the CPMC study will determine whether or not the use of variant information does indeed mitigate risk.

This external advisory board comprises highly esteemed scientists, healthcare professionals, an ethicist, and a community pastor. The concept of such a board was proposed by Dr. Kohane and colleagues<sup>30</sup>. This approach provides a model for a national system for evaluation of genome-informed medicine.

CPMC scientists review medical and scientific literature to identify candidate gene variants and provide summary reports to the ICOB. The ICOB reviews each report and votes to approve, disapprove or to request more information on each variant and condition. Factors to be considered include:

- Recommendations by the US Food and Drug Administration, Centers for Disease Control and Prevention, National Institutes of Health, National Associations for Medical Subspecialties, or other governmental advisory bodies.
- Seriousness of the disease, condition or potential adverse drug response.
- Number, size and quality of studies demonstrating a statistically significant association of a gene variant with the condition. Meta- analyses, when available, are reviewed.
- Magnitude of the effect of the particular genetic variant.
- The risks and benefits of clinical or lifestyle intervention(s) to minimize or reduce the risk.
- Data elements to measure outcomes.

Approval by the ICOB means that the association between the genetic variant and the condition has been validated and that the condition is considered to be potentially

medically actionable. Approval does not require that there be clear evidence that the variant has utility in affecting health outcomes. The goal of the CPMC is to provide the outcomes data to determine the utility of each genetic variant.

The ICOB meets at least twice per year. This frequency allows the study to integrate findings from peer-reviewed association studies for new associations and validations of prior findings. It is likely that over time, the CPMC will request the ICOB to re-review both previously rejected variants for which there is new scientific evidence and previously rejected health conditions for which prevention or treatment options have changed the potential actionability. ICOB decisions are determined by a majority vote. The group deliberations are conducted in private, assuring that scientific issues are debated in an objective, critical and unencumbered environment. However, the outcome of all deliberations is publicly disclosed through the web portal.

### **Dynamic Participant Engagement: Results Viewed Through Secure Web Portal**

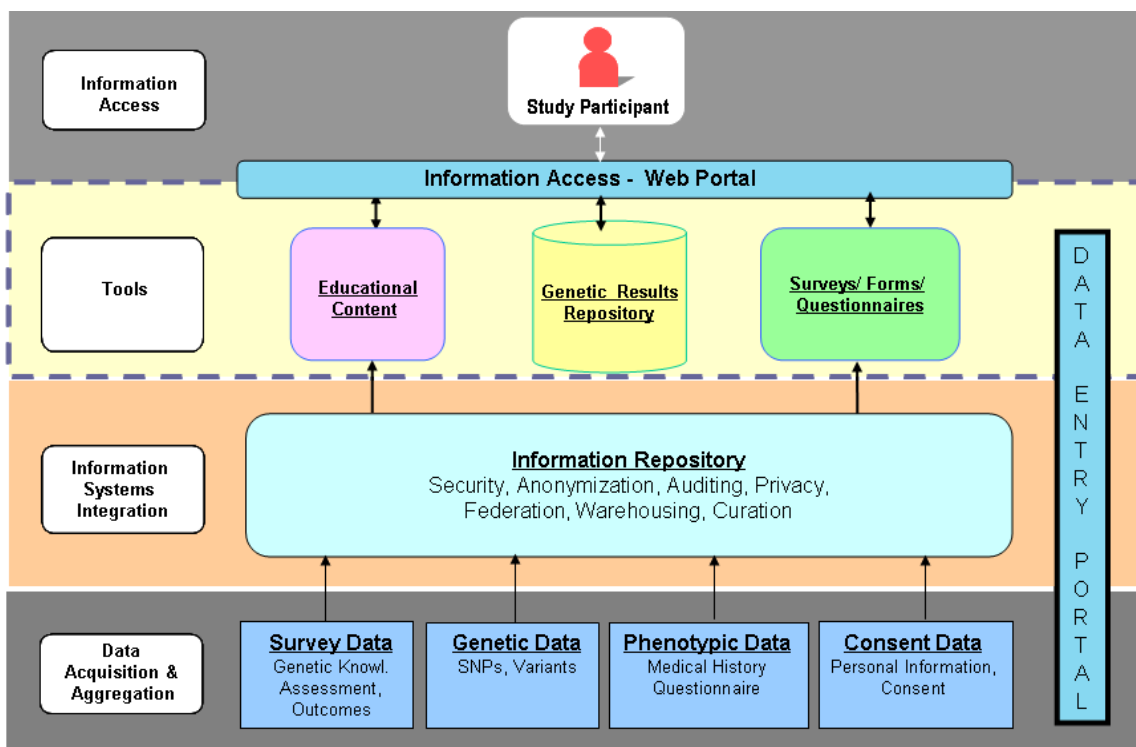
The CPMC web portal is a website with several functions. It allows for 1) data collection through online surveys, 2) genetic variant results reporting, 3) education of participants and medical professionals, 4) secure sharing of personal genetic variant information with healthcare professionals, 5) web-based requests for access to data from scientists, and 6) web-based requests for genetic counseling from participants. It is a public site with a portal for participants to log in to a secure server. In the secure portion of the site, participants may set up their CPMC account with a password, change their contact information (email address), update their consent options (e.g., opt to release their anonymized data for genome-wide association studies (GWAS)), and view their personal genetic variant information as it is released.

Additionally, the CPMC web portal has a significant amount of genetic education material. This material is written for two distinct audiences, the lay participant and the medical professional, although any individual may access the more advanced educational material if desired. The educational pages include information on basic genetics and scientific milestones such as the Human Genomic Project and HapMap project. Educational material is also provided on inheritance, cancer, the multifactorial nature of complex disease, the meaning of “risk” and how to interpret disease risk assessments, and reasons why this type of study is only possible today.

With each visit to the web portal, participants are re-engaged. Participants must elect to view each genetic variant result independently, assuring that control over the results lies with the participant and that participants are not informed of results that they are not actively seeking. Individuals who choose to view CPMC results will watch a short educational video of a genetic counselor giving anticipatory guidance for that specific variant prior to viewing their personal genetic variant information. The CPMC encourages study participants to invite their healthcare providers to view their results. Participants may authorize access to their results directly from their CPMC web portal account.

In addition, the site has current information about opportunities available to participants such as no-cost genetic counseling, educational forums and additional

surveys related to the study. There will also be the potential for the CPMC to post information about other studies for which participants may be eligible. Figure 2 provides a diagram of the information system architecture for the study.



**Figure 2.** CPMC Study Information Architecture

Important to the maintenance of participant privacy is the fact that all personally identifying information is both encrypted and stored separately from genotype and medical information. Two-factor security is used to dynamically build the web pages as participants view their personal data.

### **Realistic Risks: Explanations of the Magnitude of Risk Elevation**

The CPMC is committed to reporting realistic risks associated with genetic associations in a format that is understandable by the lay population. All results presented will illustrate the known population disease risk (specific to racial/sex/age groups, if known) and the adjusted risk based on the genetic variant genotype. Although in some cases a particular genotype may increase the risk significantly, it is expected that most genetic variants associated with complex (multifactorial) diseases will increase the risk only modestly. Until validated algorithms are available to combine risks associated with more than one genetic variant, each will be reported individually. References to the primary literature are included on all result reports.

To ensure that participants and healthcare providers understand the risks conferred by the genetic variants included in the CPMC results, an educational section of the web portal called "Understanding the Odds" has been created. This section, written for both lay and medical professional audiences, describes the concept that the risk

of complex diseases is dynamic and involves the interaction of genes with the environment. Additionally, the genetic contribution toward a complex disease is discussed, addressing the likelihood that tens of individual genes, not a single variant whose current results are being reported and viewed, influence the genetic risk of complex disease. It is also explained that given the current state of knowledge, family history is likely to be a larger risk factor for most complex diseases than any one genetic variant.

Coriell is using an additional tool to educate CPMC participants. Study participants will be invited to attend educational forums hosted by CPMC genetic counselors and clinicians from hospital partners. Upcoming events are announced to study participants through the CPMC web portal. The purpose of the forums is to educate participants about health conditions for which genetic variant information has been released as part of the CPMC study. At these sessions, the clinician will discuss the health condition; its causes (genetic and non-genetic); screening, treatment, and prevention strategies. The CPMC genetic counselor will discuss the genetic variants that are part of the CPMC study and their association with the condition, as well as the risk assessment supplied with the genetic information.

### **Understanding Results: Genetic Counseling**

Genetic counseling in the era of genomics and personalized medicine will require a new approach from traditional counseling for single-gene disorders<sup>31</sup>. Coriell employs full-time, board-certified genetic counselors who are dedicated to the CPMC study and available to provide genetic counseling to participants via email, phone and face-to-face office consultation, as well as through educational forums open to CPMC participants. Medical professionals whose patients are participating in the study may also request access to CPMC genetic counselors to discuss the study and the reported genetic variant information.

The genetic counselors will record all encounters with CPMC participants in a secure, password-protected tracking database that is only accessible to the CPMC genetic counselors. This database will allow the genetic counselors to have easy access to the history of contact between themselves and a participant. It will allow genetic counselors to track the amount of time and type of consults being made and to gather statistics on the types of diseases and variants for which the consults are being requested. This tracking system will also allow the genetic counselors to identify common areas of confusion around which future educational sessions for both the lay public and medical professionals can be tailored.

### **Medical History, Family History and Lifestyle Questionnaires**

Participants are required to complete extensive medical history, family history and lifestyle questionnaires online after establishing their personal, online CPMC account. These surveys must be completed prior to viewing genetic results. Participants will be asked to update their medical history, family history and lifestyle information one year after the information is entered and every twelve months thereafter. These data will be used for two purposes: 1) they will be used in combination with genotype data to calculate personalized risk, whenever possible, and 2) they will be used in combination with genotype data in GWAS studies to identify additional genetic

variants which contribute to complex disease and/or drug metabolism (for those participants who opted to allow their anonymized data to be used for association studies).

Coriell recognizes the importance of CPMC data in GWAS studies and has created a mechanism (via the participant consent form) for participants to indicate their willingness for their anonymized data to be shared with researchers (both from non-profit and for-profit organizations). As such, anonymized data from the CPMC will be available to all qualified researchers through the NCBI dbGaP web portal. The model is to perform surveys through the web portal, allowing cross-validation of data across questionnaires. The longitudinal nature of this project, the on-going release of genetic variant results, and the request for annual updates of survey information will allow for the collection of data that are traditionally hard to acquire, such as diet and exercise patterns over time and environmental exposures as they happen.

### **Longitudinal Data Collection: Electronic Medical Records**

Participants may opt to release recent medical records from their primary care healthcare provider via hard copy, or in electronic form if they are in a hospital partner's Electronic Medical Records (EMR) system. Updated medical records will be requested annually to ensure longitudinal data collection. These datasets will be monitored for changes in health outcomes relevant to conditions for which the CPMC has released genetic variant information. Medical records will be compared to self-reported patient medical history reports.

CPMC staff will transcribe a subset of the information in the medical record into a Personally Controlled Health Record for each participant. All Coriell information technology systems will allow compliance with established standards for interoperability (HL7) and medical data definitions such as SNOMED and LOINC.

### **Participant Privacy and Security**

Coriell has several provisions in place to maintain integrity, confidentiality and security of its data and information systems. Coriell has security policies in place to assure that all data are protected from unauthorized access and maintains audit trails, backup procedures and error checking, to assure accuracy and protection of CPMC data. Data security is a balanced combination of management and staff actions, operational activities and technological control measures. The CPMC information technology infrastructure requires three highly integrated technology layers: 1) web portal, 2) laboratory information management system for inventory management, phenotypic data management and process management, and 3) secure hardware infrastructure that contains web application servers, database servers, a storage array network, and network security appliances. Personally identifying information is encrypted and stored in a database separate from the genotype and medical data. Participants will also be required to log in to the secure web portal using their barcode identifier, username and a strong password.

### **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. Camden, NJ, the community in which the Coriell Institute is located, 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 also hosts enrollment events in Spanish and offers a Spanish version of the CPMC Informed Consent document.

### **Availability of CPMC Data to Researchers Worldwide**

The CPMC team has discussed with National Human Genome Research Institute a strategy for hosting anonymized data from CPMC participants that opt to share their data with scientists for research through the dbGaP web portal. Coriell is committed to ensuring widespread access to this valuable dataset. The Institute has a history of posting data with dbGaP for use by qualified scientists and has been involved in the return of genotypic data generated from samples in the Framingham Heart Study, as well as in the National Institutes of Neurologic Diseases and Stroke and the National Institute of General Medical Sciences repositories at Coriell.

### **Outcomes Research**

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 thorough assessment of medical history, family history and lifestyle at baseline is made prior to the release of personal genetic variant results. In addition, participants will be able to take part in other assessments, such as an examination of baseline knowledge of genetics.

When scaled appropriately, the data collected from the CPMC will be used to assess whether healthcare costs increase as a result of genome-informed medicine using objective criteria such as number of physician visits, tests ordered, data related to hospital admission, and drug prescriptions. Measures of physician practice based on surveys of physician beliefs and recommended practices will be balanced by examining choices made by participants in selection of healthcare options. Coriell will work with hospital partners to develop such metrics and with organizations such as the Technology Evaluation Center to ensure appropriate clinical data elements are monitored.

### **Summary**

The CPMC is an evidence-based research study designed to determine which elements of personal genetic data are valuable in clinical decision-making and healthcare outcomes. Medical records and genomic data will be updated dynamically. There is no charge to CPMC participants and, for participants who choose to release their data, anonymized genotypic and phenotypic data will be

made available to qualified scientists. The CPMC will enroll 10,000 participants by the end of 2009 into wellness and cancer arms. Close partnerships with area hospitals are designed to catalyze physician engagement in personalized medicine.

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