Utah's Vision for Genomic/Personalized Medicine

THE UNIVERSITY OF UTAH

Vice President for Research

201 S Presidents Circle Rm 210 Salt Lake City, Utah 84112-9011 (801) 581-7236 FAX (801) 585-6212

February 5, 2007

John Agwunobi, M.D., M.P.H., M.B.A.
Assistant Secretary for Health
U.S. Department of Health and Human Services
200 Independence Avenue S.W.
Washington, D.C. 20201

Dear Dr. Agwunobi:

It is with pleasure that I submit this joint response from the University of Utah and Intermountain Healthcare to the U.S. Department of Health and Human Services Request for Information: *Improving Health and Accelerating Personalized Health Care Through Health Information Technology and Genomic Information in Population- and Community-based Health Care Delivery Systems.*

This document describes a vision for personalized medicine and summarizes current and future activity areas at the University of Utah and Intermountain Healthcare; however, by no means is this an exhaustive list. We believe that all medicine should be personalized medicine, and that biomedical research in its entirety, from the most basic science to clinical investigation, will contribute meaningfully to the knowledge base driving personalized medicine. Utah's growing personalized medicine initiative ultimately will involve the coordinated efforts of researchers, healthcare providers, government agencies, businesses, and community-based organizations across the state.

The University of Utah holds population studies resources that are unique in this Nation and among few of their caliber in the world, thanks to the unequaled participation of Utah's citizens in biomedical research, the genealogical resources of the Church of Jesus Christ of Latter-day Saints, and their longstanding support of our federal, state, and local governments. Decades ago, these resources made it possible to identify some of the first known human disease genes. Today, they regularly produce genetic science breakthroughs that improve our understanding of human health and disease. Home to one of the nation's first electronic health records systems, Intermountain Healthcare continues to break new ground in the application of human genetic information to clinical decision support.

It is upon these invaluable resources that Utah builds its personalized medicine initiative. We are confident that continued investment by the federal government in this initiative will bring substantial returns to the health and prosperity of people throughout the United States and the world.

Please contact me if you need additional information.

Sincerely,

Raymond F. Gesteland, Ph.D.
Vice President for Research
Distinguished Professor, Human Genetics

Alan, a young father of three, was recently diagnosed with chronic myelogenous leukemia. A decade ago he would have faced chemotherapy, a bone marrow transplant, and marginal odds for survival. But today, after a simple genetic test, Alan's physician prescribes a medicine that targets the specific molecular cause of his cancer. Like most others with his diagnosis, Alan recovers completely, with renewed confidence that he will indeed be there for his children as they grow up.

This is personalized medicine today.

Imagine a yearly checkup with your family doctor. She has a computer file with your complete genome sequence and a personal profile of proteins and metabolites that influence your health. Using this information, she recommends dietary habits and an exercise plan designed specifically for you. Together, you discuss prevention methods for health issues that run in your family and make a plan for regular screening. What's more, she knows which medications will work best for you, should you need them, and which ones you must avoid. The secrets in your genetic makeup, now decoded, help you and your doctor determine what interventions will secure you the best chances for a long and healthy life.

This is the future's ultimate promise for personalized medicine.

According to the Agency for Healthcare Research and Quality, 770,000 people are injured or die each year in hospitals from adverse drug reactions (ADRs). These statistics do not include the number of ADRs that occur in ambulatory settings. Whatever the true number is, ADRs represent a significant public health problem that is, for the most part, preventable through better health care services and through better tools to predict who is at risk. Moreover, the effectiveness of prescription medications ranges from 20-60%, far below optimal.

Personalized medicine—sometimes referred to as "predictive medicine," "individualized medicine," "genomic medicine," or "information-based medicine"—is designed to improve treatments, minimize side effects, and reduce costs. These goals will be realized only when we combine intelligence and creativity with genomic resources and information technology to achieve excellence in four primary areas:

- **Accuracy**–finding better ways to design drug molecules that hone in precisely on their targets, minimizing chances for adverse reactions.

- **Efficacy**–tailoring effective health strategies to the individual, based on genetic predictors of disease risk and drug response, in the context of known environmental risk factors.

- **Safety**–matching patients with the best and safest medications for their individual physiological makeup.

- **Speed**–reducing the time and funds needed to develop effective, safe therapies.

Today we are challenged to find new ways of addressing health and societal issues that grow with our burgeoning global population: disease pandemics, adverse drug reactions, inadequate health care for the young, the old and the poor, etc. Each of these issues begs for approaches that are more intelligent, efficient, and economical than those currently in practice.

Utah's Resources for Personalized/Genomic Medicine

The ultimate promise of genomic medicine is ensuring the best possible health for every person through every phase of life. Fulfilling this promise involves much more than gene discovery and drug development. It requires the intelligent integration of data collected about genetics, biology, physiology, metabolism, and behavior, in both healthy and diseased states. It also requires information systems that can deliver the necessary information at the right time and in the right format to affect care delivery. In sum, realizing the promise of personalized medicine mandates new ways of thinking about science, health care, and public policy to ensure the best use of genomic information in tomorrow's world.

To achieve these goals, Utah is combining and leveraging the resources of the University of Utah, Intermountain Healthcare, the State, and other collaborative partners. Utah's two largest health care providers, Intermountain Healthcare and University Health Care, are respected nationally for their high-quality clinical services and systems of electronic records, which will be critical to moving forward in the science and practice of personalized medicine. Thus, the progress of personalized health care depends on strong research and health care institutions that have the ability and drive to work together.

The University of Utah

The following assets and resources of the University of Utah have been foundational in developing personalized and genomic medicine in Utah.

Groundbreaking human genetics research: Since receiving the first extramural research grant from the National Institutes of Health in 1946, the University has led the way in investigating genetic links to disease—a necessary first step toward better health strategies. Many of the key technologies for gene discovery were invented by University scientists, and more human disease genes have been identified in Utah than in any other place in the world.

Revolutionary approaches to the study of normal development and disease: Geneticist Mario Capecchi's invention of mouse gene targeting enables scientists to strategically change any gene they want in a mouse and then assess the effects of that change, thus creating accurate models for studying human development and disease.

The world's largest population studies resources: The Utah Population Database (UPDB) was established in 1975 and has established long-term partnerships with The Church of Jesus Christ of Latter-day Saints, and Utah and Idaho state cancer registries, Intermountain Healthcare, and other health care providers. The UPDB now holds approximately nine million records (see further discussion below).

A strong record in biomedical informatics: Continuing the long-standing legacy of Dr. Homer Warner, a pioneer of medical informatics and creator of one of the first electronic health records (EHR), the University currently maintains all of its patient information in UUHSC EDW, a data warehouse linked to the genealogical records of the UPDB. The Department of Biomedical Informatics has trained more Ph.D.s in Informatics than any other institution in the world.

Application of informatics to support clinical decisions. With complex data arising from genotype-phenotype interaction research, computerized information management will be essential in making personalized medicine a widespread reality. The University's approach advances clinical decision-making by focusing on new results from research on the inheritance of human diseases. It builds on approaches known to work in other domains, like the development and implementation of standards-based methods to store results from genetic tests in EHR and then use of those results in clinical decision support systems to make recommendations at the point of care. These methods must be capable of bridging the gaps between platform-independent EHRs.

The nation's first Research Park: The Research Park ensures Utah's place at the forefront of medical device and computing innovations, and it provides a home for companies associated with University technologies.

Innovative computer science and visualization: The University was one of the first four network nodes of the ARPANET, the progenitor of the modern-day Internet. Today, the Scientific Computing and Imaging Institute carries the torch with cutting-edge advances in computer image analysis.

Medical testing laboratory: Associated Regional University Pathologists (ARUP) is a University-owned company with annual revenues in excess of $250 million. ARUP Laboratories represents the single most comprehensive source of medical laboratory services in the country, including molecular diagnostic medicine and genetics. Together with the faculty of the University's Department of Pathology, ARUP consistently contributes new, peer-reviewed knowledge to medical science each year, including a suite of genetic tests.

Aggressive technology transfer: In 1960, the University became one of the first schools in the country to create a technology transfer office. Since then, the University's technology commercialization experts have helped start more than 80 new companies, creating high-salaried jobs, attracting educated people, and increasing Utah's economic vitality.

Intensive genetic services: The University complements its health care teams with perinatal, genetic, and medical genetic counseling services and training. Current practitioners, fellows in medical genetics and perinatology, and students in the genetic counseling graduate program work with families affected by and at risk for inherited diseases. They also provide diagnostic laboratory services, serve as patient advocates, and educate health care professionals and the public. The Genetic Counseling Shared Resource has operated for more than 10 years at the University's Huntsman Cancer Institute, reflecting the firm commitment to the centrality of genetic counselors in the development and execution of research protocols focused on human cancers. Cancer genetic education and counseling is an integral part of clinical and behavioral research at the University.

Ethical excellence: The University places a high priority on ethics and confidentiality in research and practice. The Resource for Genetic and Epidemiologic Research carefully governs access to data repositories, such as the UPDB. University scholars constantly analyze the evolution of policy and thought regarding ethical concerns about scientific advances.

Top-quality graduate education in medicine and research: In its ranking of America's best graduate schools for 2007, *U.S. News & World Report* named the University's School of Medicine among the top 50 U.S. medical schools in primary care and medical research.

Commitment to science education: With more than three million website visitors per year and high-caliber teacher training programs, the University's Genetic Science Learning Center (http://learn.genetics.utah.edu) is the world's most widely used resource for teaching and learning genetics.

Intermountain Healthcare

Intermountain Healthcare is a not-for-profit health system based in Salt Lake City. Serving the health care needs of Utah and southeastern Idaho residents, Intermountain's system includes 21 hospitals, numerous clinics, a health plan, and a physician group of more than 500 practitioners. In 2005, for the fifth time, *Modern Healthcare* and *Verispan* named Intermountain Healthcare the nation's top integrated health system. It has been ranked either first or second among the 500-plus U.S. integrated systems since 1999. The American Hospital Association's magazine, *Hospitals & Health Networks,* named Intermountain Healthcare in its list of the "Top 100 Most Wired" health care organizations in the country. The Health Information Resource Center awarded Intermountain Healthcare gold, silver, and bronze medals at its 2005 National Health Information Awards. These accolades reflect a commitment to a health care system that serves as the backbone for testing and implementing personalized medicine, particularly with regard to EHRs.

EHR system: In partnership with Dr. Homer Warner and the University of Utah's Department of Medical Informatics, Intermountain developed one of the nation's first large EHR systems. The Intermountain electronic data warehouse contains longitudinal medical records on nearly four million individuals, some of which go back more than 30 years. In addition to the electronic storage of information, the informatics system assists physicians with point-of-care clinical decisions for treating diabetes, community-acquired pneumonia, ventilator management, and coronary heart disease. E-resources imbedded in the EHR allow providers access to a wide range of electronic information sources, including specific genetic resources.

Quality improvement: Another critical and unique resource at Intermountain is the Institute for Healthcare Delivery Research, created in 1990 to assist Intermountain in the formal application of quality improvement techniques within the clinical care setting. Intermountain's approach to quality management has been accepted as a national model by the Hospital Research and Education Trust, the research affiliate of the American Hospital Association. Since 1992, the Institute has trained thousands of Intermountain employees and hundreds of physicians and other clinicians from across the United States and around the world in the principles of health care quality improvement. Intermountain has received top national awards for providing quality health care, including the 1996 NCQHC Quality Health Care Award. *U.S. News & World Report* ranked Intermountain's LDS Hospital as one of America's Best Hospitals in 2006 for orthopedic care, treatment of respiratory disorders, pulmonary medicine, endocrinology or diabetes care, and urology.

Intermountain's Clinical Genetics Institute (CGI)

In 2005, in recognition of the increasingly important role that genetics and genomics will play in the future of medicine, Intermountain funded CGI, which aims "To orchestrate efforts within Intermountain Healthcare to apply developments in genetics/genomics to improve the quality and value of health in the Intermountain West." CGI's mission includes:

- serving as the central genetics entity within Intermountain to direct policy making and genetic services delivery;
- coordinating clinically relevant genetics educational efforts, in both the Intermountain system and the general community;
- seeking and supporting opportunities for applied genetics research; and
- linking genomic/family medical history data to medical records in order to provide advanced genetic-based diagnostic tools for clinicians.

Through these initiatives, the Institute plans to address the rapid and dynamic changes anticipated with the addition of genomic information to the existing repertoire of clinical data used in the practice of medicine. CGI staff has a wide range of expertise, including clinical genetics, genetic counseling, health care delivery, payer issues, education, technology assessment, economic analysis, quality improvement and informatics.

As the largest integrated health system in the Intermountain West (and one of the largest in the country), Intermountain provides a wealth of opportunity for research on genetic influences in health and disease and for tests of drugs that target the products of disease-causing genes. One of the largest challenges facing personalized medicine in the future is the ability to put genetic and genomic information in the hands of providers in a useable form at the point of care. Under the leadership of Dr. Marc S. Williams, CGI leverages Intermountain's strengths in informatics, quality improvement, and clinical decision support to translate genomic discovery into clinical practice. As a pediatrician and medical geneticist, Dr. Williams has helped parents understand genetic testing results and find resources for children with genetic diseases. He and his staff serve on several national and international boards, including the American College of Medical Genetics, the Secretary's Advisory Committee for Genetics, Health and Society, the Personalized Health Workgroup of the American Health Information Community (DHHS), Ethics Subcommittee and Billing and Reimbursement Task Force of the National Society of Genetic Counselors, and the Genomics Special Interest Group of HL7.

Current CGI projects include the following:

- With grant support from HRSA through the Genetic Alliance and in conjunction with the Utah Department of Health, CGI is exploring ways to increase the use and utility of the family history through integration into the EHR.
- In conjunction with the University of Utah Department of Biomedical Informatics and Intermountain informatics, genetic information resources (both general and disorder-specific) are being integrated into the E-resources of the EHR.

- CGI is initiating a multidisciplinary Genetic Testing Practice Council to evaluate new genetic tests for utility and to develop methods to support appropriate use of new and existing tests found to have validity and utility, while erecting barriers against inappropriate tests.
- Comprehensive genetic cancer services are being developed throughout the Intermountain system, and links are being established with similar services provided at the Huntsman Cancer Institute.
- CGI is encouraging participation in didactic coursework and clinical site coordination for the University of Utah genetic counseling training program.
- A unique aspect of the CGI is the presence of a full-time analyst to address issues of new technology assessment and cost effectiveness. Partnering with other groups such as the University of Washington School of Public Health Genomics' pharmacoeconomic faculty, the Institute for Preventive Medicine, CDC, and the Economics of Genetics Technologies Seminars (organized by the Health Economics Research Centre [University of Oxford] and the North West Genetics Knowledge Park [University of Manchester]), the CGI is modifying and applying standard assessment tools within an integrated health care system.

Ultimately, Intermountain's extensive experience in implementing evidence-based medicine in its hospitals and clinics will serve as Utah's foundation for practicing genomic medicine in everyday practice.

Collaborations to Achieve Personalized Health Care

Central to the future of personalized health care is the collaboration of scientists and health care providers from diverse research and practice settings to address the challenges of incorporating scientific evidence into best clinical practice. Utah has fostered several key relationships, described below, to achieve this goal.

The Utah Population Database

The Utah Population Data Base (UPDB) is the only database of its kind in the United States and one of few such resources in the world. Created in 1975 and initially derived from extensive family records of the Church of Jesus Christ of Latter Day Saints, UPDB is a set of Utah family genealogies linked to cancer information and death certificates. The UPDB has grown into a rich research resource that contains a wealth of information for genetic, epidemiologic, demographic, and public health studies and is maintained as a statewide resources under the stewardship of the Huntsman Cancer Institute. Investigators have used this resource for more than three decades to identify and study families with a high incidence of cancer or other diseases in order to analyze patterns of genetic inheritance and identify specific genetic mutations. The UPDB integrates datasets received from the Utah Department of Health (UDOH), the Utah Cancer Registry (an NCI SEER-funded state-wide registry), the Cancer Data Registry of Idaho, and the Driver License Division, Utah Department of Public Safety. It includes records on cancer, cause of death, and medical details associated with births. Since many of the data sets in the UPDB receive annual electronic updates, the UPDB is a dynamic and constantly improving database. It has a long history of generating new meaningful data resources by linking disparate data sets together.

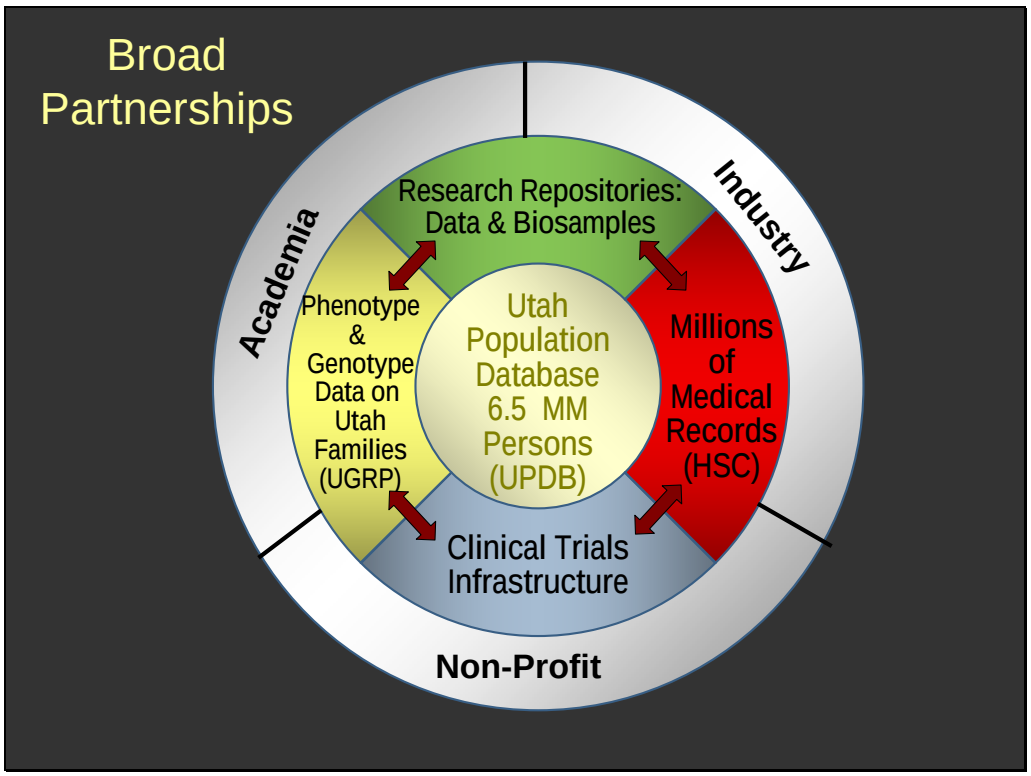
The UPDB includes information on more than 6.5 million individuals and family history data on almost 4 million individuals, representing pedigrees that span up to 11 generations. Most families living in Utah are represented in the UPDB. Extensive studies have demonstrated that the Utah population is not inbred and is representative of populations of Northern European origin.

Recently, a link was established between UPDB and the medical information contained in the Enterprise Data Warehouse at the University of Utah Health Sciences Center Data Resource Center, which contains information on more than 1.7 million patients. This has expanded the ability of investigators to address questions associated with the inherited basis of human diseases and traits.

Collaborating with investigators from the University of Utah's College of Social and Behavioral Science, 5.9 million addresses were geo-coded to Universal Transverse Mercator coordinates, allowing researchers to locate individuals in U.S. Census tracts. In addition to analytical approaches for familial clusters of disease, researchers can now apply spatial modeling techniques, including geographic information systems analysis.

Finally, leadership of the UPDB and the UDOH are working to develop a new, long-term collaboration that would integrate two extremely large data repositories (described below). Claims data that are part of statewide, administrative databases would be linked with and integrated into UPDB. The claims data cover a period from 1996 to present and include more than two million records from hospital inpatient discharge, about two million records from ambulatory surgery, and more than five million encounters with the emergency department. Information on linked records would be returned to UDOH, allowing both institutions to conduct research that is not currently possible.

To fully realize the potential of the UPDB, it is essential to be able to link these powerful genealogy databases with rich clinical data. This facilitates the identification of phenotypes of interest occurring in families. These families can then be contacted to participate in research designed to identify underlying genetic causes. To this end, an agreement in principle has been established between the University of Utah and Intermountain that will allow linkage between the UPDB genealogy and the medical records contained within the Intermountain EHR for specific research projects. Details currently are being negotiated that will allow contribution of this rich phenotypic data to research while ensuring compliance with all relevant statutes regarding privacy of personal health information and adherence to the highest ethical standards of biomedical research.



Source: Stephen M. Prescott, M.D., President, Oklahoma Medical Research Foundation. former Executive Director of the Huntsman Cancer Institute. Keynote Address, Why Personalized Medicine, Why Utah. Governor's Vision Conference, December 6, 2006.

As a complement to the UPDB, the Utah Health Family Tree project has collected data on family histories that have been clinically validated. It represents the largest collection of validated, self-reported family history data in the United States. Analysis of these data has allowed development of risk stratification algorithms for several common diseases, with the possibility to further examine the data to refine existing algorithms and apply these techniques to other disorders. Combining this information with the genomic discoveries will give insight into the interactions between environment and the genome—an essential element of personalized medicine that is currently poorly understood.

Sharing Statewide Health Data for Genetic Research

One successful approach in identifying human disease genes for complex disorders is the identification of large families of related individuals that have a predisposition to a specific disease. The high degree of relatedness of the DNA of family members permits the analysis to focus on minor factors, allowing identification of genes that are minor contributors to a disease in question. Key to this sort of genetic analysis are highly unique populations, like those found amongst larger-than-average-sized families in Utah, strong genealogical records, and a high likelihood of continued local residence. Researchers also would benefit from population-wide information, which would permit identification of all individuals in an area with a common disease history for a disorder. It would be ideal to have access to population-wide information on environmental factors and exposures encountered by individuals who later develop disease to examine in conjunction with population-wide genetic information.

Claims data that are part of administrative databases at UDOH can be used to provide information on diagnosis. These include datasets such as hospital inpatient discharge records, ambulatory surgery data, and emergency department encounters. Genealogical records and linked birth certificates that are part of the UPDB will provide family structure. To integrate these data, a methodology is being developed that allows data to be shared, linked, and maintained in UPDB. Access and training would be provided to researchers. This would actualize the ideal meshed dataset of genealogies/family histories, medical records, and vital statistics, all collected on a population-wide basis. Such a shared dataset would be an unparalleled resource for genetic studies of human disease, one in which virtually any common human disease can be analyzed to identify the genes responsible for the disorder.

The development of population databases that combine health and genetic data has taken on a new focus. Many believe that such databases are crucial to unlocking the genetic basis of common diseases. There is an ongoing set of ethical questions associated with database models that combine disparate sources of information about individuals. The University of Utah has focused its attention on privacy issues raised by linking computerized data and has been attentive to the need to protect privacy while facilitating research. It also has reviewed the deCODE Genetics, Inc. model that integrates medical data with genealogy and molecular genetic information within a for-profit organization. Having an intermediary between data contributors and data users, such as that used by the UPDB, serves as a mechanism by which privacy and confidentiality can be protected in the linking and use of computerized datasets in biomedical research.

LineaGen Research Corporation

Headquartered in Salt Lake City, LineaGen Research Corporation (LineaGen) is a Utah non-profit, 501(c)3 research and licensing organization that was formed by the University of Utah, the State of Utah, and the Huntsman Cancer Foundation. Its goal is to provide access to the assets of the UPDB through fostering and enabling collaborative projects with University of Utah researchers.

LineaGen is using the power of population genetics and Utah's leadership in human genetics research to personalize medicine by leveraging a comprehensive biomedical research repository that integrates biological samples with medical and genetic information from both population-based and multigenerational family studies. LineaGen's key asset is its ability to facilitate commercial access to research using the UPDB, an unmatched integration of vital statistics, clinical records, and genealogical information. LineaGen utilizes this powerful population genetics discovery platform to identify and validate biomarkers, coordinate clinical trials, and identify health-promoting and disease-causing genetic factors.

Through ongoing collaborations with LineaGen, University of Utah researchers are continually recruiting and collecting detailed clinical data from affected individuals in many genetic disease areas. In addition to this extensive phenotype collection, each patient provides a DNA sample and relevant tissue samples. Researchers are using these samples for additional phenotype analysis, including proteomic and metabonomic profiling, and for comprehensive genotyping analysis. LineaGen researchers have created a two-pronged approach to discovery research—genomics and genetics. The genomic approach compares phenotype and genotype in large, unrelated case and control populations. The genetic approach compares phenotype and genotype within large Utah families. In addition to groundbreaking genomic and genetic research, LineaGen clinical researchers

are performing stratified clinical trials. Utilizing the UPDB and related assets, clinicians are able to rapidly identify, stratify, and recruit clinical trial populations.

With corporate partners, LineaGen sponsors research programs designed to discover novel biomarkers, clinically validate known biomarkers, and better understand biological pathways of human health and disease through the identification of causative or associated genetic factors. Typically, each program begins with the recruitment of patients by practicing care providers and thorough phenotypic characterization of their disease and disease history. Every examination includes collection of relevant biosamples, which are available via licensing agreements to LineaGen's research partners. Following patient recruitment, LineaGen initiates analysis of the samples combined with the clinical data. Sample analysis may include, but is not limited to proteomic analysis, metabonomic analysis, case/control association studies, linkage studies, and data mining. LineaGen is continually seeking partners to license intellectual property in many areas of genetic research, fund ongoing discovery research projects, and launch new discovery research programs.

The Utah Genetic Reference Project (UGRP)

Identifying the genes contributing to common diseases such as cardiovascular disease, neurological illnesses, and cancer has been difficult, partly because the genetic mechanisms of these diseases are complex. The involvement of multiple genes in disease pathogenesis, variable penetrance of gene expression, and non-genetic factors that influence genetic activity (i.e., the environment) are all factors that make the discovery of genes for common diseases much more challenging. Unraveling the genetics of complex diseases within the context of large, extended families will facilitate the discovery of biomarkers important to personalized medicine. University of Utah scientists have set their sights on identifying genes for common diseases and quantitative traits (e.g., blood pressure, bone mineral density, blood test results) that may be used as early markers of disease.

An important genetic resource at the University of Utah that can contribute to advances in personalized medicine is the UGRP. This project is a gene mapping initiative aimed at identifying quantitative trait loci and genes underlying common human disease. The UGRP uses an extensive collection of phenotypic data that it has collected on 42 large, multi-generational Utah families to search for genes and biomarkers associated with susceptibility to human diseases. These unique Utah families were originally recruited in the 1980s as part of a worldwide effort to create genetic maps of the human chromosomes. These genetic maps enabled scientists to identify hundreds of genes predisposing humans to disease.

Since then, the UGRP has created an extensive registry of phenotypic data collected from each family member to complement the vast amount of genotypic information on these Utah families. This phenotypic data was collected in a standardized manner in the Huntsman General Clinical Research Center. It includes individual medical histories, clinically relevant tests, such as blood pressure, pulmonary function testing, and cardiac ultrasounds, and biochemical measurements. The UGRP demonstrates the ability to 1) collect a wealth of clinical and phenotypic information on extended families and 2) share this data with numerous national and international scientists. These families can be readily expanded into even larger family pedigrees with up to 10,000 individuals by linking them to the UPDB. Important gene discoveries from the UGRP can easily be extended and confirmed in such larger families.

The International HapMap Project is an NIH-funded initiative that recently completed a haplotype map of the human genome which describes the common patterns of human genetic variation. This project utilized the UGRP families as their reference source for the Caucasian population. The results of this scientific undertaking, which developed a highly detailed view of common DNA variations, will facilitate genetic comparisons among the different peoples of the world and most importantly, be utilized to determine why some of us are more genetically susceptible to (or protected from) certain diseases.

Genealogy Enabled Network and Integrated Information Environment

The University of Utah houses a vast amount of medical data that is used by researchers and clinicians to perform cutting-edge medical research. While the data used to perform research is currently distributed among various sources within the University, the University's long-term goal is to integrate clinical information with biomedical research data—including pathology notes, genotypic and phenotypic information and other clinical notes and records—to facilitate research studies by automating the collection, preservation, security, and retrieval of research data.

The University of Utah and its affiliates, including the Huntsman Cancer Institute, are in a distinct position to leverage the invaluable information assets present in the state. As such, the University of Utah is embarking on an initiative to build a comprehensive clinical research environment. This environment will integrate clinical, genotypic, phenotypic, and genealogy information in a centralized data management environment to enhance analytic capabilities at the University of Utah. The objective is to extend the environment across the University's research enterprise and, ultimately, to other collaborating institutions. The ultimate goal is to transform and improve the traditional way that health care is delivered, via personalized medicine. To that end, the University of Utah seeks to achieve the following broad objectives:

- Establish an extensible and replicable Information Technology (IT) foundation for clinical data management and research via a federated database management environment.
- Create a web-based, front-end application to facilitate:
    - data collection and dissemination,
    - multi-dimensional analysis,
    - clinical data mining, and
    - statistical analysis.
- Develop and implement IT and health care standards in clinical data management.
- Shape the translational research process via IT by standardizing clinical records and developing new pieces of IT solutions in data mining (e.g., front end, data model, reference architecture).

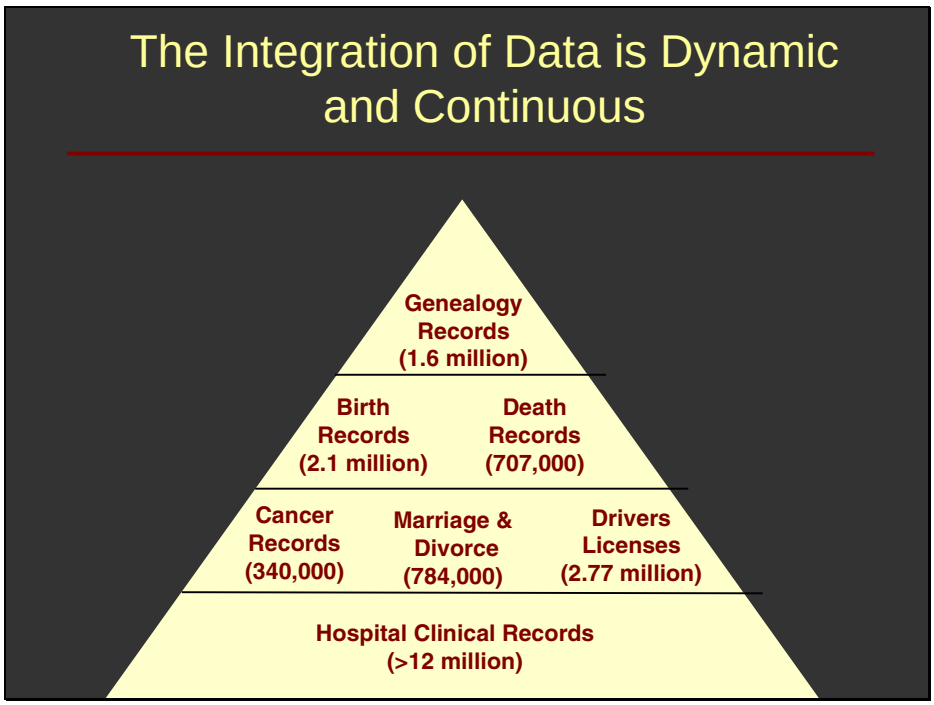
In support of these objectives, the University of Utah seeks to advance the quality of patient care and physician and patient interaction by: 1) developing information-based technologies to provide appropriate patient data; 2) advancing linkage between patient information and clinical research in the broad area of genotype and phenotype information, with patient information consistent with the University of Utah's statutory requirements under the Health Insurance Portability and Accountability Act of 1996; and 3) providing linkages to extend the created clinical portal to ad-hoc query specifications for private and public sources designed with the goal of high-quality patient

diagnosis and treatment recommendations. Thus, it is forming strategic collaborations in the realm of digital health care and medical research systems with a focus on personalized medicine.

Because University of Utah Health System medical information is not stored in UPDB, the ability to query specific diseases and family information simultaneously is not currently possible. To address this issue, a collaboration was formed among IBM's Healthcare and Life Sciences and Business Consulting Services and informatics groups across the Health Sciences Center. In 2005, a conceptual design was completed titled *Genealogy Enabled Network and Integrated Information Environment (GENIIE)* or *GENIIE: Detailed Design Plan and Specifications Document*.

The University of Utah Health Sciences Center Data Warehouse system will be used to provide information on diagnosis using ICD9 codes, encounters, events, and outcomes. Family Structure information will be sourced from the UPDB. GENIIE will lay the foundation for developing an integrated, robust clinical information platform to serve as the foundation for the enterprise-wide environment across all areas of the University and other related clinical research initiatives. GENIIE will enable users to identify disease trends, predict and quantify the characteristics of illnesses, and provide results for publication. This environment encourages the identification of opportunities to increase levels of care and scopes of treatments. Some of the possibilities that have already been identified include:

- By using information collected during routine medical visits and incorporating it with other disease-related information, one can use statistical methods to forecast disease incidence and prevalence.
- There is significant disparity in the way individuals respond to medications in terms of toxicity and treatment efficacy. The variability in drug effects includes the pathogenesis, clinical variables, and severity of the disease being treated. Examples of these variables include the individual's age, gender, nutritional status, and habits such as smoking. It is now recognized that inherited differences in the response of the patients to drugs or perhaps even surgical procedures, such as grafts, could be linked to genetic, physiological, and anatomical differences among the patients.
- Combining patient demographics, clinical data, and genetic information will provide opportunities to depict relationships that will help researchers link their findings to clinical outcomes.



Source: Stephen M. Prescott, M.D., President, Oklahoma Medical Research Foundation. former Executive Director of the Huntsman Cancer Institute. Keynote Address, Why Personalized Medicine, Why Utah. Governor's Vision Conference, December 6, 2006.

Examples of Focused Personalized Medicine Efforts

Research advances already are providing opportunities to practice personalized medicine. Examples of focused efforts in specific disease areas, using specific tools and techniques, are described below.

Elucidating the Genetics of Colon Cancer

Colon cancer affects 6% of the U.S. population, or 1:17 individuals. Approximately 700 new colorectal cancers are diagnosed in Utah each year. The risk of colon cancer in first-degree relatives of patients with large bowel cancer is two- to three-fold greater than risk in the general population, and familial clustering of colon cancer accounts for 20-35% of all colon cancer diagnoses. However, colon cancer syndromes for which the causative gene is known only account for 2% of all colon cancer diagnoses. The remaining inherited susceptibility requires genetic definition to improve screening, prevention, and management and to elucidate molecular mechanisms of susceptibility. The "low-hanging fruit" has been picked, and the remaining inherited susceptibility has proven much more difficult to define due to complex genetics.

For many years, clinicians and laboratory scientists from Utah have studied cancer genetics and cancer risk in families using the UPDB. Utah pedigrees have been a key resource for identifying cancer genes. More importantly, these large families have allowed for clinical characterization of genetic syndromes and provided for the development of guidelines for clinical management. Clinical and molecular information also has been applied to the population as a whole. Genes that are

mutated in the inherited cancer syndromes are often mutated in sporadic, population-based cancers, and understanding these genes is important for defining prevention and treatment approaches in the more common setting.

Clinical information collected from these studies leads to valuable clinical recommendations. For example, surveillance and prevention guidelines are focused on a much younger population and tend to be more aggressive for first-degree relatives of those with breast or colon cancer than surveillance and prevention for the general population.

Of all the cancer genetics programs at the University of Utah, the colon program is the most advanced in resources and serves as prototype for research that can be accomplished with these resources. The University of Utah's Familial Colon Cancer research study includes 51 kindreds, DNA from 533 individuals, and colonoscopy data on 347 individuals, all accompanied by detailed medical, diet, and family history. The Familial Colon Cancer Registry enrolls individuals from families with increased risk of developing colon cancer and those who have or are at-risk of developing a known hereditary polyp syndromes or HNPCC. The Registry has two primary functions: 1) to create a research resource from which investigators can draw potential study participants and 2) to serve as an educational resource for participants, their physicians, and other health care providers.

Researchers and physicians have collected surplus surgical tissue on 587 colons, including 307 samples of colon cancer, for research purposes. De-identified clinical information linked to these tissues is available in a secure database, and staging and outcomes from the cancer registry will be added. Fresh RNA is stored on 234 fresh colonic biopsies, and corresponding RNA expression data is stored on a subset of these. In addition, matching tumor and normal DNA have been extracted from more than 400 high-risk colon cancer cases (diagnosed under age 50 or two first-degree relatives with colon cancer).

The Utah Cancer Registry is a partner in these efforts, which have established protocols and methods for contacting eligible participants. Continued work with the Utah Cancer Registry will permit development of a large resource of cancer cases for high-density SNP genetic association studies. Associated SNPs can be compared with data from the large families to identify meaningful genetic variants. Integration of this data with the UPDB will in turn permit investigators to capture familial relationships.

Investigators intend to answer the following research questions using these resources:

1. What genes/genetic variants increase/decrease risk of cancer?
2. What genes/genetic variants affect responses to chemotherapy?
3. How common are genetic variants in the population?
4. What is the actual increased risk from different genetic variants?
5. What is the value of a personalized medicine approach?
6. How should genetic variants be used to test for increased risk and to identify molecular targets for intervention?
7. What modifies risk (environmental factors, genetic factors, chemopreventive agents)?
8. How should genome-based clinical testing be offered? Under what clinical setting? To whom? Would it affect medical decisions?
9. How can screening and prevention strategies be developed around genetics and genomics?

Using Extended Pedigrees to Study Autism

A common complex disease that serves as an example of current work in Utah is autism. Once thought rare, a new 14-State prevalence study funded by CDC reports that 1 in 133 Utah children have an autism spectrum disorder, ranking Utah 3rd highest in the Nation. This study was conducted in partnership between the state Department of Health, the Autism Research Program of the University Department of Psychiatry, and CDC. In addition, the Utah Autism Research Program has used the UPDB to build large extended autism pedigrees for gene-mapping studies. A 10K marker genome scan of the first pedigree was published in 2006, giving significant linkage for a locus on chromosome 3. This extended family includes seven members with autism and is the largest published autism pedigree in the world literature. Five other similar pedigrees have been ascertained and are under investigation. The long-term goal of the Utah Autism Research Program is to combine the UPDB with longitudinal data collection, information technology, sophisticated medical imaging and visualization, and targeted medication delivery systems to build capacity for:

- early and rapid diagnosis using medical tests specifying not only that a child has autism but also specifying the neurobiological subtype of autism.
- detailed understanding of abnormal molecular and developmental neural circuit events specific to each child and each type of autism.
- identification of specific genetic and environmental causative factors specific for each child and family and prevention.
- individually tailed specific treatments delivered directly to abnormal areas in the brain, specific to each type of autism.
- prevention of multiple complications of the disorder and associated medical and psychiatric comorbidity and knowledge of which medications, if needed, will be most effective and have the lowest risk of adverse side effects.
- specific recurrence risk individualized for families.
- identification of families at high risk and preemptive interventions.
- increased capacity of health care providers to evaluate and treat more children
- a huge decrease in the burden of autism on families and society and huge cost-savings in health care dollars,
- children and families empowered and given hope for the future.

Interdisciplinary Approaches to Understanding Substance Abuse

Drug abuse/addiction is a complex biomedical condition resulting from interactions among genetics, individual factors, and environment. Addiction occurs in the brain and affects specific brain structures that control memory, learning, motivation, decision-making, and mood. Addictions are implicated in the progressions of many cancers, auto accidents, hospital admissions, emergency room visits, gastrointestinal problems, child and adolescent health care concerns, and co-morbid psychiatric conditions. Addiction is a chronic, progressive, and relapsing disease that can result in death if not recognized and treated, costing society billions of dollars each year.

The University's Utah Addiction Center (UAC) is committed to identifying which genetic, individual, and environmental variables contribute to pathogenic decision-making as it relates to addiction, so that interventions can be developed to modify risk variables. At present, the UAC is

focusing on personal pathogenic decision-making through the Program for Drug Abuse Research Translation (PDART). By understanding the cognitive process of "how" and "why" individuals make decisions related to substance use and health, investigators hope to develop effective interventions. The UAC is probing the heritability of addiction to identify potential candidate genes linked to the addiction process. This research is coordinated with animal model work designed to identify specific receptor subtypes and mechanisms involved in addiction.

Several members of the PDART have worked with the University of Utah Center for Human Toxicology to measure drugs and their metabolites for drug abuse-related research projects, including methylphenidate, cocaine, and amphetamine analogs (e.g., METH, amphetamine, MDMA, and related metabolites). Specifically, this research investigated issues such as tolerance, sensitization and neurotoxic mechanisms.

Using Imaging Technologies to Tailor Treatment

Imaging technology is causing a revolution in modern health care. Imaging experts now have a range of imaging technologies at their disposal to assist in diagnosing disease, characterizing its severity and extent (staging), and even predicting response to various forms of therapy. Images are rendered in three dimensions, allowing physicians to view a problem from all angles. For example, using MRI alone, it is now possible to visualize blood vessel networks, the "wiring" of the brain (white-matter tracts), specific brain activities, and the functions (fMRI). MRI and PET can assess the perfusion of the heart. MRI and PET can detect tumors and define many important characteristics of a tumor, such as the efficiency of the tumor blood supply—essential to the prescription of effective therapy. PET using an appropriate tracer makes it possible to define biochemical activities within a tumor, for example, how fast the tumor cells are using up energy (sugars) or oxygen (metabolism), or how rapidly the cells are dividing and growing (proliferation). Radiologists can now provide details of anatomical, physiological, and metabolic parameters. Equipped with this knowledge, surgeons, cardiologists, and oncologists can tailor treatment to the precise features of a disease in a specific individual. The advantage of medical imaging is that relevant biologic information is gathered non-invasively. It is therefore possible to monitor the progression of a disease over time.

One goal is to develop non-invasive imaging techniques to identify relevant biological parameters of disease to improve therapeutic selection and monitor response to subsequent treatment. For example, a complementary set of imaging techniques can characterize the blood supply, growth parameters, metabolic characteristics, and cell surface receptors of a tumor. These biologic parameters can be used to help select the most appropriate therapy based on biologically relevant information. Once the therapy is selected it can be assessed and monitored early in the course of therapy to ensure that the patient is receiving the most appropriate therapy. In those instances where the biologic parameters are not behaving as expected, another course of therapy can be chosen, thus ensuring that every patient is receiving the most appropriate therapy for his or her particular tumor.

This "personalized" early therapeutic monitoring of therapy will then correlate with tumor response and can be used to predict a final treatment outcome. Currently, the outcome of a treatment is only known at the end, or even long after the end, of a particular treatment course. The goal is to ensure early in the course of a particular therapy that there is an appropriate biologic response. Using the results of these various imaging tests, it will be possible to pre-select the most appropriate treatment and modify drug treatments, interventions, or therapeutic procedures accordingly during the therapy of the individual patient.

Drug Development Science

The University of Utah Departments of Pharmaceutics, Pharmacology, Pediatrics, Medicinal Chemistry, and Bioengineering have been exploring the opportunity to develop a joint Institute for Drug Development Science. This Institute would focus on advancing the science applied to the drug development process while creating infrastructure that would aid investigators in this critical translational stage from bench to bedside.

The significant intellectual energy that has produced great advances in drug discovery over the last decade has not been equally applied to the drug development process. This creates a bottleneck, whereby new discoveries are slowed in their progression toward patient care because our technology, understanding, and abilities in assessing the most promising compounds for clinical application are limited. Further compounding this problem, the process of clinical evaluation of new drugs has been extremely expensive and inefficient because information learned along the drug development process is not fully integrated into subsequent development phases. This lack of translation leads to a need for large, time-consuming clinical trials that exponentially increase the cost of drug development.

In a report on the Critical Path Initiative, the Food and Drug Administration identified six primary areas to be addressed in improving the drug development process. These include three specific points of focus at the University of Utah: 1) development of new biomarkers and disease models, 2) streamlining clinical trials through improved design and conduct, and 3) exploiting bioinformatics for model-based drug development. The University of Utah has a unique opportunity to address these opportunities by catalyzing existing resources, including:

- The Translational Critical Path Initiative (TCPI) is funding infrastructure and development for preclinical toxicology, pharmacokinetics, dosage scaling from animal models to humans, and supporting the development of new therapeutics, vaccines, and diagnostics toward regulatory submission for initiating clinical trials for emerging infectious disease.
- The Anticonvulsant Drug Development Program, which will create animal models of disease.
- The Pediatric Pharmacology Research Unit, which is funded to conduct and support clinical trials of therapeutic agents with specific emphasis on children.
- The Center for Human Toxicology, which will develop high-precision bioassays for measuring drug and biological substrates and conduct projects to develop new biosensors and companion diagnostic products in the areas of pediatric pharmacology and infectious disease.
- The Pharmacokinetic and Pharmacodynamic Modeling Resource will work with all the components of the Institute. In essence, these resources will work in concert to provide computer simulation and modeling for planning clinical trials and incorporating biomedical knowledge developed in the preclinical phases of drug development. In particular, work on developing companion diagnostics using biomarkers and assays developed in the preclinical phase are powerful in "personalizing" clinical trials so that the right drug is tested in the right population.

The Brain Institute

A main research goal of the University of Utah's Brain Institute is to facilitate discovery of new genetic influences on normal brain function and common brain diseases. Genetic variability is a

major source of differences in brain anatomy and physiology that contributes to individual differences in personality, cognitive functions, and susceptibility or resistance to many psychiatric and neurological disorders. Brain imaging methods are increasingly valuable in assessing individual differences in brain anatomy and physiology and creating objective endophenotypes for the characterization and diagnosis of brain disorder subtypes. Over the past two years, the Brain Institute has helped departments across the University of Utah campus hire new brain imaging scientists. A current effort is recruiting scientists interested in using the UPDB resource and imaging-based phenotyping to conduct family studies of the genetics of common psychiatric diseases. A research community capable of combining genetic and imaging approaches to advance understanding of multiple brain disorders is rapidly developing in Utah. A likely outcome of this development is the discovery of new genes related to disease resistance and susceptibility and new biomarkers (genetic or image-based) useful in prevention, diagnosis, and treatment.

Summary: Essential Components of Utah's Genomic/Personalized Medicine Initiatives

Utah's efforts in building the foundations for personalized medicine include wide-ranging and long-term investments in research and infrastructure.

Basic Research

Breakthroughs in prevention, diagnosis and treatment will require more thorough knowledge of the biology underlying both health and disease. Thus, a successful genomic medicine initiative must lay a strong foundation in several research areas, including:

- **Genomics.** Analyzing DNA sequences from humans and other organisms enables scientists to discover new genes involved in health and disease and learn how they work.

- **Proteomics.** Encoded by our genes, proteins comprise the thousands of moving parts in the intricate machines that are our cells. Investigating how these parts interact with each other—and what happens when parts don't work properly—will lead to new disease therapies and targets for drug development.

- **Metabolomics.** The human "metabolome" is the complete set of chemical metabolites that emerge from biological processes in our bodies. Assembling and comparing metabolic profiles of health and disease will lead to identification of therapeutic targets and, ultimately, to customized health strategies for every patient.

- **Animal models of human disease and disease development.** The human genome shows amazing similarity to those of other animals, from mice to fish and even fruit flies and worms. This means that other animals get diseases similar to ours, and through studying them we can develop better health strategies. Advanced genetic methods enable scientists to create disease-causing mutations in model organisms, study their effects and test new treatments.

- **Phenotyping human disease and wellness.** With the completion of the Human Genome Project, application of discoveries has been impeded to some extent by a lack of attention to the expression of the genomic information (i.e., the phenotype). Phenotypes such as "asthma" or "diabetes" are too general for in-depth study, as evidenced by the slow progress of discovery in association studies. Establishing reliable, quantitative measures for complex neurological and psychiatric disorders is especially challenging. The extensive medical records available through the University of Utah and Intermountain Healthcare and the expertise being developed by University of Utah scientists can greatly facilitate the analysis of phenotypes, particularly when linked to a resource such as the UPDB or Utah Health Family Tree. Linkage of this rich phenotypic data with the abundant '-omic' data above will greatly increase the pace of medically relevant discoveries.

- **Population studies.** The UPDB and The Utah Family Tree will enable unprecedented advances in each of the areas described above and provide a starting point for testing new clinical applications as they emerge.

Technology and Clinical Applications

Programs in the following areas will ensure the timely translation of scientific advances to real-life technologies and clinical applications.

- Pharmacogenomics will coordinate studies of candidate drugs to assess how they influence genes, proteins, and metabolic profiles in different people.

- Biomedical informatics is the backbone on which all breakthroughs in genomic medicine will be made. It also represents the only hope of distilling the massive amount of genomic data into clinical messages that can support best care practices. We must ensure that all partners in a genomic medicine initiative have the most advanced data analysis and knowledge management tools to enable their best work.

- Technology development will accelerate the creation of better research and clinical tools.

- Clinical research and application will deliver new knowledge and protocols to support clinical decisions and patient care across the care continuum from the quaternary referral hospital to the individual physician office.

- Genetic counseling services and research will help patients understand how their genes influence their health and provide access to the latest resources in genomic medicine.

- Novel education methods will create a health care workforce that is knowledgeable and capable of delivering this radically new approach to care.

Core Facilities

Centralized facilities are required to support research and clinical operations, such as:

- Gene expression profiling, which can determine how gene expression differs in tissues under different physiological conditions or following administration of a medication—a technique that can be used to develop biomarkers for disease

- Genotyping methods, including SNP and microsatellite analysis and DNA sequencing, to determine genotypic variation among human populations and in animal model genomes

- Phenotyping methods, to correlate genetic profiles with quantitative and precise measures of traits in both health and disease states

- High risk clinics, to enroll eligible participants into research studies and provide support for individuals and families with an increased risk of developing a disorder or disease

- Sample banking, to accurately and safely store DNA, tissue, and other biological samples donated by study participants

- Research computing, to support data collection and analysis, facilitate knowledge transfer, and ensure access to research tools

- Subject recruitment and oversight, to ensure the safety of research and clinical study participants.

Ethics, Law, and Policy

At the core of genomic medicine lies one of humanity's most personal attributes: our genetic code. Thus, research and clinical advances emerging from a genomic medicine initiative must pass careful scrutiny by ethicists, legal professionals, policymakers, and the public. The genomic medicine initiative must provide an interdisciplinary venue for individuals from many disciplines to assemble and analyze ethics, law, and policy issues related to genomic medicine, and it must ensure that ethical principles are adhered to in research and care.

Education, Training, and Outreach

Education, training and outreach are an immediate product of genomic medicine research programs. New discoveries might take years to translate into better medications or technologies, but they can be applied in the forms described below to help people today.

- Health professions and genetic counseling education can provide health care providers with the knowledge and tools they need to promote personalized medicine.

- Research training can be implemented to help meet our nation's critical need to develop science and engineering talent.

- Public outreach should be encouraged to share information about research and clinical advances with broad audiences, helping to improve quality of life for people around the world.

International Collaboration

To create maximum benefit for humanity, the talents of partners worldwide must be leveraged while strengthening relationships within our global community. Genomic medicine initiatives must foster relationships with global partners in all program areas. One such positive relationship has been established by the Public Population Program in Genomics (P3G), a consortium formed to support knowledge sharing across the international population genomics community. P3G promotes a common understanding of ethical, legal, social, public health and policy issues in genomic medicine and information sharing between countries. Already, four major programs have joined P3G: The United Kingdom's Biobank, Quebec's CARTaGENE, the GenomEUtwin project from Finland, and the Estonian national gene bank project. Utah, with its valuable population and medical database resources, can play an important role in this new international venture.

The participation of Intermountain Healthcare in the Economics of Genetics Technologies Seminar, which has participation from countries world-wide, will be instrumental in learning about the economic impact of these emerging technologies, as well as providing knowledge from implementation within a health care system that is not nationalized.

Acknowledgements

Raymond F. Gesteland, Ph.D.
Vice President for Research
Distinguished Professor
Human Genetics
University of Utah

Mark F. Leppert, Ph.D.
Professor and Co-Chairman
Eccles Institute of Human Genetics
University of Utah

Marc S. Williams, M.D., FAAP, FACMG
Director
Intermountain Healthcare Clinical Genetics Institute

John R. Hoidal, M.D.
Professor and Chairman
Department of Internal Medicine
University of Utah School of Medicine

Grant M. Wood
Senior IT Strategist
Intermountain Healthcare Clinical Genetics Institute

John M. Hoffman, M.D.
Professor of Radiology and Neurology
Director of Nuclear Medicine, Department. of Radiology
Director, Molecular Imaging Program, Huntsman Cancer Institute
Medical Director, Utah Center for Advanced Imaging Research
University of Utah School of Medicine
Investigator, The Brain Institute at the University of Utah

Chris Johnson, Ph.D.
Distinguished Professor of Computer Science
Director, Scientific Computing and Imaging Institute

Steven E. Kern, Ph.D.
Assistant Professor
Department. of Pharmaceutics and Pharmaceutical Chemistry
University of Utah College of Pharmacy

Janet E. Lainhart, M.D.
Associate Professor of Psychiatry
University of Utah School of Medicine
Member, The Brain Institute at the University of Utah

Jennifer Logan, Ph.D.
Director of Strategic Communications
The Brain Institute at the University of Utah

William M. McMahon, M.D
Professor of Psychiatry
University of Utah School of Medicine
Member, The Brain Institute at the University of Utah

Geraldine P. Mineau, Ph.D.
Director, Population Sciences Program
Huntsman Cancer Institute
Research Professor, Department of Oncological Sciences
University of Utah

Joyce A. Mitchell, Ph.D.
Professor and Chair
Department of Bioinformatics, School of Medicine
University of Utah

Thomas N. Parks, Ph.D.
Professor and Chairman
Department of Neurobiology and Anatomy
Executive Director
The Brain Institute at the University of Utah

Karl V. Voelkerding, M.D.
Medical Director
Advanced Technology Group
Institute for Clinical and Experimental
Pathology
ARUP Laboratories
University of Utah

Christopher L. Sans, Ph.D.
Business Development Manager
LineaGen Research Corporation
Technology Commercialization Office
University of Utah

Terri Pianka
Coordinator of Development Research
Office Of Sponsored Projects
University of Utah

Stephen M. Prescott, M.D.
President
Oklahoma Medical Research Foundation

Gregory M. Jones, Ph.D.
Science Advisor to the State of Utah

Project Manager

Rick Mandahl, M.B.A.
Director of Business Development
The Brain Institute and
Office of the Vice President of Research
University of Utah