Improving Outcomes, Reducing Costs
The Partnership for Personalized Medicine (PPM) addresses two critical issues in health care: improving patient outcomes and reducing health care costs.

Health care expenditures throughout the world are rising to unprecedented levels, while aging populations represent an increasing disease burden for both individuals and the broader community. Technological and biomedical breakthroughs have significantly advanced medical practices; however, the cost of therapeutics continues to spiral upwards. Optimizing treatment for patients remains an ongoing challenge, with uncertainties in identifying disease risk, diagnosing disease onset and selecting appropriate therapies.

PPM presents a fresh approach to the health care predicament, with a collaborative model that engages health care professionals, policy makers and researchers in the discovery, development and validation of diagnostic biomarkers. New diagnostic biomarkers that improve early disease detection and predict treatment responses will better inform clinical decisions for individual patients and, in doing so, improve the efficiency and effectiveness of health systems. Partners participating in PPM may also have an opportunity to further develop their own biotechnology capacity in diagnostics. PPM provides a unique opportunity to invigorate and revolutionize health care worldwide. We invite you to join us on this exciting and groundbreaking journey.

Executive Summary

The Partnership for Personalized Medicine (PPM) addresses two critical issues in health care: improving patient outcomes and reducing health care costs.

Health care expenditures throughout the world are rising to unprecedented levels, while aging populations represent an increasing disease burden for both individuals and the broader community. Technological and biomedical breakthroughs have significantly advanced medical practices; however, the cost of therapeutics continues to spiral upwards. Optimizing treatment for patients remains an ongoing challenge, with uncertainties in identifying disease risk, diagnosing disease onset and selecting appropriate therapies.

PPM presents a fresh approach to the health care predicament, with a collaborative model...
Science and technology are beginning to provide revolutionary insights into medicine through a comprehensive molecular understanding of human health and disease. However, the promise of better health for all is undermined by the growing cost of medical treatments, which threatens the very viability of health care systems around the world. By 2015, health care spending in the U.S. is expected to reach $4 trillion, or 20% of GDP, and by 2020, spending will double in OECD countries. The challenge we face is to use our new knowledge to improve patient outcomes while stabilizing or reducing the costs of health care.

We believe that this is possible by realigning our science to meet the needs of health care.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Disease</th>
<th>Annual cost ($US)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avastin</td>
<td>Colon cancer</td>
<td>$52,000</td>
</tr>
<tr>
<td>Avastin</td>
<td>Lung, breast cancer</td>
<td>$100,000</td>
</tr>
<tr>
<td>Gleevec</td>
<td>Leukemia</td>
<td>$31,000</td>
</tr>
<tr>
<td>Herceptin</td>
<td>Breast cancer</td>
<td>$36,000</td>
</tr>
<tr>
<td>Rituxan</td>
<td>Lymphoma</td>
<td>$50,000–$156,000</td>
</tr>
<tr>
<td>Erbitux</td>
<td>Variety of cancers</td>
<td>$120,000</td>
</tr>
</tbody>
</table>

Source: USA Today, July 11, 2006

Current economic incentives assure that companies will develop the most expensive new therapeutics and devices while neglecting the power of new diagnostics to improve health at reduced cost.
The promise of personalized medicine to improve health care outcomes and reduce health care costs will not be manifest by the marketplace where incentives align with expensive therapeutics for late-stage disease. It is paramount that health care providers and insurers play a new role in medical research, becoming the vehicle for the discovery, validation and implementation of new diagnostic platforms that can achieve the goals desired by patients and providers – prevention, early detection and effective intervention at reasonable cost.

Critical opportunities exist in all diseases for better molecular diagnostics to improve patient outcomes while reducing health care costs:

- **Risk assessment**: Identifying individuals at greater risk of developing specific diseases will enable the implementation of preventive measures that could eliminate both the suffering from disease and the costs associated with treatment.
- **Early detection**: For many diseases, diagnosis at earlier stages of disease progression allows intervention when there is a greater likelihood of effective treatment and cure. For example, in nearly all forms of cancer, early diagnosis can lead to a cure at a fraction of the cost of ineffective treatments for late-stage disease.
- **Definitive diagnosis**: The diagnosis of many diseases is challenging due to a lack of distinctive symptoms. Improved diagnostics will allow more rapid and effective implementation of appropriate treatments for those who will benefit while preventing adverse side effects and the costs of treatment for those who will not.

Archimedes said, “Give me a lever long enough and a fulcrum on which to place it and I shall move the world.” The lever that will help you and your health system move health care in a revolutionary new direction is the Partnership for Personalized Medicine (PPM).

**Breast Cancer Treatment**

Breast cancer: Treatment for early-stage, hormone-responsive cancer

- Surgery to remove tumor
- Hormone therapy

- **20% of patients** require additional chemotherapy (high risk of recurrence)
- **80% of patients** do not require additional chemotherapy (low risk of recurrence)

**Source**: Burrill Personalized Medicine Report, November 2007

---

**Five-year Survival From Diagnosis, According to Stage at Diagnosis**

<table>
<thead>
<tr>
<th>Stage at Diagnosis</th>
<th>Five-year Survival Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Localized</td>
<td>100%</td>
</tr>
<tr>
<td>Regional</td>
<td>90%</td>
</tr>
<tr>
<td>Distant</td>
<td>70%</td>
</tr>
</tbody>
</table>

**Source**: National Cancer Institute Surveillance Epidemiology and End Results (SEER)

http://seer.cancer.gov/faststats/
Accessed December 10, 2007

---

**Cervical Cancer Costs**

<table>
<thead>
<tr>
<th>Stage at Diagnosis</th>
<th>Direct cancer-related costs per patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Localized</td>
<td>$19,665</td>
</tr>
<tr>
<td>Regional</td>
<td>$34,796</td>
</tr>
<tr>
<td>Distant</td>
<td>$92,547</td>
</tr>
</tbody>
</table>

**Source**: Helms et al., Medical Care, 1999
PPM is a nonprofit initiative with substantial foundation support whose goal is the development, validation and clinical application of new molecular diagnostics, designed to improve health outcomes and, importantly, reduce health care costs.

Partnership for Personalized Medicine is led by Dr. Lee Hartwell, President and Director of the Fred Hutchinson Cancer Research Center and 2001 Nobel laureate; Dr. Jeffrey Trent, President and Scientific Director of the Translational Genomics Research Institute (TGen); and Dr. George Poste, Director of the Biodesign Institute at Arizona State University.

How Does the Partnership for Personalized Medicine Work?

Our model is based on the formation of collaborative partnerships that leverage a full suite of genomic and proteomic capabilities provided by PPM with dedicated health care systems to complete demonstration projects that integrate four key elements:

- A cohesive and interactive partnership between health insurers, providers, clinicians, and researchers;
- Epidemiologic, clinical and economic analysis to identify critical intervention points in disease management;
- Systematic and empirically based discovery, development and validation of new diagnostic tests to improve patient outcomes and reduce system costs; and
- Collaborative, prospective and evidence-based evaluation of the test within health systems to validate and implement the new test in patient management.

An Evidence-Based Approach

PPM features the following approaches:

Health care economics:

Economic analysis will identify major disease costs and opportunities for interventions to reduce costs; examples include earlier disease detection to enable preventive measures, and testing to avoid unnecessary therapy for patients who will not respond to therapy.

Decision Tree for Disease Management

Clinical progression of disease

- Risk assessment
- Early detection
- Diagnostic evaluation
- Treatment

Risk for disease: Disease onset, preclinical phase

- Symptoms
- Early intervention
- Precise diagnostics
- Targeted therapy

Avoid disease
Cure or stop progression
Diagnosis

Economic benefits

- No treatment costs
- Treatment cost savings for early vs. advanced disease
- Avoids costs of inaccurate diagnosis
- Avoids costs of treating persons who will not respond to therapy

REduced costs of disease
Improved productivity
Partnership for Personalized Medicine

In the current health care paradigm, the cost-effectiveness of a diagnostic test is generally not evaluated until after implementation, if at all. Thus PPM introduces a new approach whereby economic models drive diagnostic development.

**Clinical management:**
Following consultation with clinical experts, PPM will construct decision trees to outline current treatment management. A decision tree will enable PPM to identify steps in disease management that would benefit from improved diagnostics. The value of a new diagnostic will lie in its ability to better facilitate clinical decisions and prompt an appropriate intervention to improve patient outcomes. Based on models utilizing clinical, epidemiologic and economic data, the performance criteria needed to both improve outcomes and reduce costs will be decided by all partners, including insurers, providers, clinicians, and scientists.

**Biomarker discovery:**
Research clinicians in the health care system will identify appropriate patients, obtain tissue or blood samples and record clinical outcomes. PPM will use these samples to identify hundreds of biomarkers that distinguish diseased individuals from healthy individuals. An iterative process between clinicians, patients and PPM will locate biomarkers that are sensitive and specific for the desired point of disease intervention. Markers that meet agreed upon performance criteria will move forward in the development pathway into clinical testing.

**Implementation:**
After prespecified performance criteria have been demonstrated by prospective analysis of patient and economic outcomes, the new test will be introduced into clinical care. The insurer will then reimburse for the test. Patient outcomes will continue to be tracked, providing opportunities to further enhance test performance.
Why now?
The Science of Molecular Diagnostics

With the completion of the human genome came great expectations for personalized medicine. It was thought that discovery of genetic variations that confer significant risk for major diseases would permit the widespread adoption of preventive measures and focused screening for early disease detection. The promise has not materialized. In fact, except for rare mutations, most common genetic variations associated with prevalent diseases confer very small risk for disease. Transcriptomics, the analysis of the activity of genes in different tissues, has shown improved diagnostic capability but is complex, and clinical correlations have been difficult to reproduce. Both genomics and transcriptomics will continue to inform medical science and occasionally provide useful clinical information, but their ultimate role in personalized medicine remains uncertain.

The Promise of Proteins

Recent advances in proteomics and improvements in mass spectrometry now make it possible to identify and quantify proteins at previously undetectable levels. This opens new opportunities for the development and application of protein biomarkers across a broad range of disease areas. It is these advances that lead us to believe that dramatic new opportunities in molecular diagnostics are at hand. Proteins are more informative than DNA or RNA as diagnostics and can be applied to a broader spectrum of diseases for a number of reasons:

- DNA reveals only hereditary predisposition, whereas proteins change dynamically in response to physiological conditions and can reveal disease onset and progression as well as lifestyle and environmental risk exposures.
- A single gene can produce a family of 10 to 100 variant proteins. This variation adds to the amount of information available from the spectrum of proteins.
- Proteins from diseased tissue are found in the bloodstream, whereas DNA and RNA are generally obtained by biopsy of the disease tissue itself. Therefore, clinicians can measure protein biomarkers by a simple blood test that is much less invasive than tissue biopsy.
Protein biomarkers will also be useful in the further development of medical imaging tools such as X-rays, magnetic resonance imaging (MRI), ultrasound and positron emission topography (PET). Combining protein biomarkers with imaging technology will enable the precise identification of disease activity within the body. However, imaging tests are expensive. Therefore, using less costly blood-based protein diagnostics as an initial step to identify which patients require imaging tests will also contribute to the reduction of health care costs.

Technology and Proteomics Production Facility

To effectively facilitate the development of diagnostic tests, PPM draws upon the strengths of two of Arizona’s leading bioscience entities, the Biodesign Institute at Arizona State University and the Translational Genomics Research Institute (TGen). PPM will integrate the shared expertise of these entities in proteomics, biomarker discovery, cell biology, and bioinformatics, with each bringing specific capabilities and facility resources to the collaboration. An industrial-scale, high-throughput proteomics facility will be uniquely positioned to serve as a hub for biomarker discovery. PPM will employ state-of-the-art technology platforms and research in supercomputing, nanotechnology and health economics, as well as genomics, transcriptomics and tissue sampling.

Technology Sharing

Initial discovery and development work for demonstration projects will take place at the Biodesign Institute, TGen, Fred Hutchinson Cancer Research Center and other collaborating institutions. However, technological innovations and knowledge may also be transferred to partners. Should a partner wish to establish a facility in their own country, PPM would provide support for such a venture through training and advice. This arrangement will allow partners to leverage the initial project into new disease areas, with the potential for further improvements in health care and cost savings.
The Benefits of Partnership

Partnering with PPM will offer a number of valuable benefits and opportunities:

• Our partners will be participants in applying health care economics in their settings to find cost-effective solutions to disease management. These solutions, combined with the application of information technologies to track patient outcomes that are correlated with molecular diagnoses, will be integrated into the cycle of creativity.

• Our partners will be collaborators in the effective use of genomics and proteomics to identify those at risk for disease, detect the presence of early-stage disease, match the needs of individual patients to effective therapy, and monitor for disease recurrence.

• Our partners will join an expanding network of health care systems and laboratories dedicated to transforming the practice of medicine through the application of molecular knowledge to patient care. Partnership will provide a unique opportunity for learning, innovation and solution sharing.

• Our partners will be able to establish their own diagnostic technology centers, enabling them to stay at the forefront of the health care revolution. We are dedicated to helping our partners establish their own technology capability by providing advice, best practices and training.

• As knowledge and improved methodologies become available to medicine, there will be an increasing need for governments, insurers and health care providers to develop robust policy for implementing change. Through the auspices of the Pacific Health Summit (www.pacifichealthsummit.org), our partners will have a forum for ongoing policy development.

An Invitation to Revolutionize Health Care

We invite you to partner with us in our effort to move the world toward revolutionary new diagnostic tools that will enable your patients to live healthier, more productive lives while reducing the overall costs of health care.
The Partnership for Personalized Medicine is made possible by the generous support of The Virginia G. Piper Charitable Trust and the Flinn Foundation.

Partnership for Personalized Medicine Leaders

Lee H. Hartwell, Ph.D.
President and Director
Fred Hutchinson Cancer Research Center
2001 Nobel laureate

Dr. Hartwell is President and Director of Seattle’s Fred Hutchinson Cancer Research Center and Professor of Genome Sciences at the University of Washington. Dr. Hartwell is a member of the National Academy of Sciences and received the Albert Lasker Basic Medical Research Award, the Gairdner Foundation International Award, the Alfred P. Sloan Award in Cancer Research and the 2001 Nobel Prize in Physiology or Medicine for research on the fundamental processes that underlie cell division.

George Poste, D.V.M., Ph.D., F.R.S.
Director
Biodesign Institute at Arizona State University
Del E. Webb Distinguished Professor of Biology
Chief Executive Officer, Health Technology Networks

As director of Arizona’s largest cross-disciplinary research institute, Dr. Poste draws on four decades of diverse experience in molecular biology, pharmaceutical development, personalized medicine, and biosecurity. The Biodesign Institute at Arizona State conducts results-oriented research to address challenges in personalized medicine, global public health, the environment, and national security.

Jeffrey M. Trent, Ph.D.
President and Scientific Director
Translational Genomics Research Institute (TGen)

Dr. Trent is President and Scientific Director of the Translational Genomics Research Institute. TGen’s mission is to make and translate genomic discoveries into advances in human health. The joining of science and medicine in this fashion has created a new research vision—a bench-to-patient bedside perspective that is changing how we look at illness.

Prior to forming TGen, Dr. Trent served for ten years at the world’s largest biomedical research institute—the National Institutes of Health in Bethesda, Maryland. There, he founded and directed the laboratory division of the federal agency in charge of coordinating and finalizing the Human Genome Project.

Dr. Trent is the author of over 300 manuscripts in the scientific literature, has received numerous honors and awards, and sits on the editorial boards of a dozen scientific publications.
“Gaining diagnostic access to illness at the deep, molecular level allows for medicine to become not only personalized but also predictive … which moves the name of the game from the treatment of illness to aggressive promotion of wellness. The shift … will revolutionize the health care system … especially when we consider costs …”

—G. Steven Burrill
The Journal of Life Sciences, May 2007