Examples of NIH Research Advances and Economic Benefits

Advances Related to Genomics

Personalizing Treatment Decisions for Breast Cancer. In the past, women diagnosed with breast cancer and negative lymph nodes have faced a vexing decision – whether or not to proceed with chemotherapy. After lumpectomy and radiation, rigorous NIH studies have shown that most women are already cured – but not quite all, and the small additional increase in cure rate with chemotherapy has still motivated most women to go through this grueling and expensive experience. The Human Genome Project has now provided tools to make this decision much more personalized. Molecular testing of the breast cancer cells, using a gene-based diagnostic called OncotypeDx, now makes it possible to see which genes are turned on or off in an individual tumor. That pattern of gene activity allows prediction of the chance of recurrence at high accuracy. This genomic test will be used this year by approximately 50,000 women. A large fraction will be found not to need chemotherapy. They will avoid a brutal experience, and our health care system will be spared $100M in costs for therapy that is not needed.

Genomics Allows Better Prescribing. Toxicity is one of the major hurdles to overcome in the successful development of new drugs. Here's an example where genomics has solved that vexing problem: FDA approved the drug Abacavir as a key element in a promising new approach to treat HIV infection in 1998. However, despite the dramatically improved clinical outcomes, some patients suffered a severe hypersensitivity reaction (high fever, skin rash, even death) to the drug. Genomic analyses in the years that followed revealed a particular genetic sequence that was associated with the bad reaction to the drug. Recommendations to test the DNA of patients prior to prescribing Abacavir were added to the FDA label in 2008, reducing hypersensitivity reactions almost to zero and generating cost savings -- as patients could now safely be prescribed the safest and most effective drug for their treatment. This new field of using genomics to choose the right drug at the right dose for the right patient at the right time now applies to more than a dozen drugs, and is called "pharmacogenomics".

Genetically-Targeted Therapeutic Development. Most drugs in the past have been developed through trial and error. Now, with growing information about the molecular basis of disease, stemming from the genome project, it is possible to design drugs that go right to the vulnerable target of the disorder. A recent example is the development of a new drug (known so far by its technical names PLX4032, or vemurafenib) for malignant melanoma, the most deadly form of skin cancer. The drug was specifically designed to block the effects of a gene called BRAF, which was shown by DNA sequencing (reading out the letters of the code) to be dangerously overactive in most cases of melanoma, driving the malignant process. The drug has caused melanoma tumors to shrink significantly in nearly half of the subjects, reduced the risk that the disease would progress by nearly two-thirds, and reduced the chance of dying by 63 percent. Interestingly, a form of leukemia not previously connected to melanoma also has been shown to have the same genetic fault in BRAF, and may respond to the experimental drug with a similarly promising success rate.

Genome Sequencing to Diagnose the Undiagnosed. About 7000 rare diseases are known to affect humans. Taken together, such rare disorders constrain or shorten the lives of more than 25 million Americans. But only about 200 currently have therapies available. The tools provided by the Human Genome Project have led to the discovery of the precise cause of almost 4000 of these conditions in just the last few years. Even more importantly, for an increasing number of those disorders, knowledge of the basic DNA defect has led to entirely new approaches to treatment. As just one example, children with the rare and heartbreaking disease progeria suffer from premature aging. They age at seven times the normal rate, dying of heart attacks and strokes at an average age of 13. Discovery of the molecular cause has led

to a clinical trial of a drug (originally developed for cancer) that is showing promise of slowing or stopping the course of the disease.

Mobilizing Rapid Public Health Responses. Foodborne infections of bacteria, such as the *Escherichia coli* outbreak in Germany this spring that killed almost 40 people and sickened more than 2,000 others, or the emergence of dangerous human viruses like the one that caused the Severe Acute Respiratory Syndrome (SARS) epidemic in 2003, are biological puzzles that can have devastating public health and economic implications. Using genomic technologies developed in the aftermath of the Human Genome Project, investigators now quickly determine the DNA sequence of bacterial and viral pathogens, enabling the development of diagnostic kits to confirm incidents involving the infectious strain of interest and inform public health officials and policymakers about intervention strategies to track and contain any associated consequences of the epidemic.

Advances in Other Research Areas

Universal Flu Vaccine. Every year, influenza kills more than 36,000 people and hospitalizes 200,000 more. NIH researchers are closing in on a universal flu vaccine that would protect against multiple strains of influenza for extended periods of time and do away with the costly, time-consuming process of making, distributing, and administering millions of seasonal flu vaccines. A two-step vaccination strategy has already been able to protect animals against multiple strains of influenza. Ongoing small scale human clinical trials are assessing the safety and efficacy of this vaccine approach, and will allow scientists to identify vaccine candidates to move forward into large-scale trials.

Preventing Type II Diabetes. A recently completed 10-year follow-up study of participants in the landmark NIH Diabetes Prevention Program has found that early intensive lifestyle changes (diet and exercise, aided by training and behavior modification skills) reduced the incidence of type II diabetes in high risk individuals by 34 percent. The benefits of the lifestyle change were especially pronounced in participants age 60 and older. Implementing this program in standard medical practice, now being discussed between NIH and CMS, could save millions of lives and hundreds of billions of health care dollars.

Low Dose CT Screening of Lung Cancer Saves Lives. Lung cancer is the most common cause of cancer deaths in the United States and the world. In most cases, however, lung cancer is not detected until symptoms appear—usually after the disease has spread beyond the lungs, at which point long term survival is rare. Data from an NIH-sponsored National Lung Screening Trial demonstrated that screening with low-dose helical CT scanning results in 20 percent fewer lung cancer deaths among current and former heavy smokers. This development marks the first time that a screening test has been found to reduce mortality from lung cancer.

Prevention of Preterm Birth. Babies born too early, i.e., before 37 weeks of gestation, face a host of health problems from acute, life threatening complications including respiratory distress syndrome, to hemorrhaging in the brain, to long-lasting deficits such as vision and hearing loss and developmental disabilities. In the past decade, the rate of U.S. preterm delivery among first time mothers has increased 50 percent. NIH research has now shown that a synthetic form of the naturally occurring hormone progesterone can cut the risk of preterm birth by 45 percent among women at risk. This advance may help reduce the substantial economic burden of preterm birth, which is estimated to be $26 billion per year.

Anti-Retroviral Treatment to Prevent HIV Infection. Each year, approximately 56,000 Americans become infected with HIV; globally, the annual number of new infections is roughly 2.6 million. NIH

sponsored landmark clinical trials that successfully demonstrated the effectiveness of anti-retroviral drugs. Those trials also led to the conclusion that treatment of HIV-infected pregnant women could significantly reduce transmission of HIV from mother to child, thereby decreasing the global infection rate, alleviating human suffering, and reducing mortality and costs associated with life-time treatment. Recently and dramatically, NIH research has demonstrated that early treatment can be a primary strategy to prevent further infections. It is entirely possible that applying universal testing and early treatment of HIV positive individuals could end the epidemic in the U.S.

Examples of Economic Benefits of NIH Research

NIH Research Has a Significant Impact on the Economy of Communities, Regions, and the Nation at Large

- NIH is a catalyst and powerhouse for creating and maintaining economic growth across the U.S. As documented by the United for Medical Research's *An Economic Engine,* in 2010, NIH funding:
    - led to the creation of 487,900 quality jobs;
    - produced $68.035 billion in new economic activity; and
    - allowed 16 states to experience job growth of 10,000 jobs or more.

- A published report, the *Economic Impact of the Human Genome Project,* prepared by the Battelle Technology Partnership Practice, estimated a stunning $796 billion in economic benefits to the U.S. from the initial federal investment of $3.8 billion in the Human Genome Project. That's a 141 to 1 return on investment. In 2010 alone, human genome sequencing activities generated $67 billion in U.S. economic output, $20 billion in personal income for Americans, and 310,000 U.S. jobs.

NIH Research Drives Innovation and Supports the Global Competitive Stature of the U.S.

- NIH research and discoveries have led to dramatic growth in the field of medical innovation. These industries innovate and compete by leveraging NIH research and knowledge. As documented in *An Economic Engine*, the medical innovation sector:
    - employs almost 1 million people and pays total wages of $84 billion as of 2008; and
    - exported $90 billion of goods and services in 2010.

- But as U.S. support for biomedical research has been effectively flat since 2001, other countries are clearly gaining ground.

    - On June 29, 2011, the European Commission proposed to increase spending on research and innovation by about 45 percent over the next seven years. The proposal includes three main objectives: excelling in science, meeting "grand challenges," and improving competitiveness.

    - Although NIH led the human genome project starting in 1990, successfully mapped the human genome by 2003, and continues to discover many causes of genetic diseases, China has now taken the lead in genome sequencing. At the end of this year, the Chinese genomics center in Shenzhen, BGI, will have the world's largest next-generation sequencing capacity. It will:
        - surpass the DNA sequencing capacity of the entire U.S.;
        - represent a third of the world's sequencing capacity; and,
        - be able to sequence an individual's genes for less than $10,000.

- A report called the *2011 Global R&D Funding Forecast*, sponsored by Battelle, showed a declining U.S. research commitment relative to our GDP, even as other nations increase their investments in research and life sciences.

    - In 2011, it is projected that Israel (4.2%), Sweden (3.3%), Japan (3.3%), and South Korea (3.0%) will spend a greater proportion of their gross domestic products on R&D than will the U.S. (2.7%).
    - Recently, China and India are increasing their expenditures in R&D by about 9 percent per year.