



THE IMPACT OF GENOMICS ON THE FUTURE OF HEALTH CARE

by Lynne Williams

The Human Genome Project was truly a remarkable accomplishment. When the project was “finished” April 14, 2003, it not only was ahead of schedule, but also under budget (particularly unusual for a government-sponsored program). One must also consider that scientists were able to go from Watson and Crick’s initial description of the structure of DNA in 1953 to a complete mapping of the entire human genome in less than 50 years!

There is no question that the practice of medicine in the post-Human Genome Project (or “Genomic Health Care”) will be significantly different from the current practice of medicine. Up to this point in time, “traditional” genetic medicine has been an area where geneticists looked at a single gene and the effect(s) which polymorphisms or mutations of that gene have on a given patient. The new field of “genomics” looks at the entire human genome and how multiple genes interact with each other, as well as with environmental factors.

Identifying specific genetic alterations that impact human physiology/pathology is not clear-cut. We know that 9 of the 10 leading causes of mortality have genetic components (heart disease, cancer, cardiovascular disease, chronic lower respiratory disease, diabetes, pneumonia/influenza, alzheimer’s disease, kidney disease, and septicemia), although

the exact genetic contribution in most cases remains unclear. We have also recognized that there are not only genes that predispose to certain diseases, but also genes that protect an individual from getting a particular disease. However, it is technically more difficult to identify genes that protect us from diseases than to find genes that make us more susceptible.

The real challenge facing the health care system is to translate genome-based knowledge into workable health care applications and benefits. In order to do this, we must:

1. develop workable strategies to *identify* genetic contributions to disease and drug response
2. develop strategies to identify gene variants that contribute to *good health* and disease resistance
3. develop genome-based approaches to *predict* disease susceptibility and drug response, enabling early detection of disease (i.e. develop what would basically be a molecular taxonomy of disease states)
4. use our new understanding of genes and pathways to develop new therapeutic approaches
5. explore how genetic risk information is conveyed in clinical settings to improve health outcomes and reduce cost
6. develop genomics-based tools that improve the health of all (i.e. we must avoid socio-economic stratification of the results of genomics-based medicine)

The incorporation of genomics into medicine will change health care by creating a fundamental understanding of the biology of many diseases, even many “non-genetic” ones. For example, why does Mr. Jones, who has smoked 3 packs of cigarettes a day for 60+ years, live to be 93 years old? What genetic factors in his make up allow him to detoxify carcinogens that we know to be in cigarette smoke?

Genomics will change health care by redefining disorders by their mechanism of causation, rather than simply by

symptoms. For example: asthma, as a disease, is often at least partially diagnosed by wheezing (a symptom), and is treated with accepted asthma medicines. However, some affected individuals respond to these treatments, while others do not. Why? The effectiveness of the asthma therapies may depend on the actual molecular/genetic cause(s) of the asthma. The ability to identify the exact etiology, and the correlation of this information with drug sensitivity/resistance would allow clinicians to more accurately prescribe treatments.

Thus the knowledge of individual genetic predispositions will allow clinicians to treat individuals as individuals. Again— not every woman necessarily needs a yearly mammogram to screen for breast cancer, and not every man needs PSA levels (prostate specific antigen) to screen for prostate cancer. There are genetic components of an individual's physiology which may predict which individuals are at greatest risk for developing these diseases, and for whom more frequent screening may be appropriate. For others, less frequent screening may be acceptable. Being able to predict pre-test likelihood will result in substantial financial savings for the health care system.

It is important to realize that genes by themselves are not completely predictive—that environmental influences are still incredibly important. However, the ability to institute pre-symptom medical interventions based on genetic-susceptibility screening (e.g. antihypertensive agents before hypertension develops, or anti-colon cancer agents before overt colon cancer occurs) should significantly reduce morbidity and mortality.

Another important medical arena in which genomics will likely play a role is the area of pharmacogenomics. Understanding the interface between genomics and pharmacology will allow new approaches to drug design. It will also allow the development of individualized medication schedules based on genetically determined variation in both therapeutic effects as well as adverse side effects to specific medications. It may well also lead to the development of new medications for specific

genotypic disease subtypes. We may be able to predict who will have a positive response to a certain drug, who will have no response, and who will have adverse side effects, based on the genetic makeup of key enzymes in the genetic pathways that metabolize the drug. We may also be able to predict when we can use higher doses of a drug, with a better response or cure rate, because the patient won't have undesirable side effects. Thus genomics will likely change health care by allowing both individualized prognosis, as well as treatment.

Will the health care system of the future be one in which Mrs. Smith goes to her physician, to be told "Let's check your genome". One buccal swab and a battery of tests later, the physician has genetic sequence data on a long list of genes known to variably affect a myriad of diseases!?!

The real challenge facing the health care system, in terms of the effects of genomics on society, will be incorporating genomics to maximize the benefits and minimize the harms, of access to this incredible information. It will be absolutely essential that society develop public and political policy options regarding the uses of genomics in both medical and non-medical settings. We must carefully define the ethical boundaries for the various uses of genomics. Importantly, we must not over-interpret the information obtained from genomics, as in most cases it will reveal a "tendency" and not necessarily a "prediction".