The Hurdled Race Toward Personalized Medicine: The Study of Pharmacogenomics – An interview with Dr. Stan Bardal

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The completion of the Human Genome Project in April of 2003 signaled the beginning of the "genome era," and pharmacogenomics has been heralded as one of the first major clinical applications of the striking advances that have occurred in its wake.[1] A blend of clinical pharmacology and human genetics, pharmacogenomics aims to characterize the variability of individuals' responses to drug treatments, where phenotypes can range from life-threatening adverse drug reactions to an equally serious lack of therapeutic efficacy.[2,3] Dr. Stan Bardal is a faculty member with the UBC Medical Undergraduate Program and a member of the Therapeutics Initiative. He holds extensive knowledge in the field of pharmacology and pharmacogenomics. In an interview, he provided insight into the changing role of pharmacogenomics in medicine.

In discussing whether clinical genomics and personalized medicine will realistically enhance drug therapy, Dr. Bardal mentioned that the practicality of pharmacogenomics depends on how the immense amount of data on genetic polymorphisms and their drug interactions is presented to physicians and practitioners (S. Bardal, personal communications, November 15, 2012). At a time when for as little as $299, private companies will sequence entire genomes and provide health and trait reports, access to genetic information is easy; however, the number of variants and their potential effects during treatment with different drugs is growing exponentially (S. Bardal, personal communications, November 15, 2012). As a result, Dr. Bardal emphasized the role of information technology in making information about a patient's pharmacogenetic response accessible without increasing the complexity of the physician's already multifaceted decision-making process (S. Bardal, personal communications, November 15, 2012).

According to Dr. Bardal, the greatest use of pharmacogenomics thus far has been in cancer therapy. He elaborated that, since "cancer is a disease so rooted in genetics," it is becoming more routine to "look at the genetic composition of a tumor and its receptors," in addition to histology, for diagnosis and therapeutic action. In most other fields of medical practice, however, it seems that pharmacogenomics has not yet had a serious influence, because of a gap in the knowledge of genetic basis of many illnesses. As such, there is no way to predict, based on a patient's phenotype, whether a drug will have a variable response.[3,4] There is, however, one particular exception: a blood thinner known as warfarin has been shown to influence the efficacy and the therapeutic index of the drug based on a patient's genotype (S. Bardal, personal communications, November 15, 2012).

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In discussing the benefits of pharmacogenomics, Dr. Bardal was quick to highlight improvements in the safety of drug therapy. He went on to explain that although most people with different polymorphisms can have appropriate responses to a drug, "the 1 out of 50 patients whose response may be disastrous will affect the therapeutic choices for the other 49," and so, pharmacogenomics will empower physicians to prescribe therapies with improved safety and efficacy. In addition, Dr. Bardal believes that pharmacogenomics will drive drug discovery, because more companies will work to develop drugs for people with a particular polymorphisms. On the other hand, he highlighted that one of the main disadvantages of pharmacogenomics is the potential for people to be targeted or ostracized because of their genetics. For example, if 5% of breast cancer patients have a polymorphism that limits their choice to one particular drug, there might not be financial incentive for pharmaceutical companies to develop such a specific therapy. Alternatively, more tailored drugs may be more expensive than those used for widespread polymorphisms (S. Bardal, personal communications, November 15, 2012). Another concern is genetic discrimination, which is particularly disconcerting in the United States, where private insurers could

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refuse patients because of their genetic composition (S. Bardal, personal communications, November 15, 2012).

According to Dr. Bardal, scientists in Canada, and more specifically British Columbia, are among the leaders in the field of pharmacogenomics. While the claims for the immediate impact of pharmacogenomics can be sensationalized in the media, its ultimate significance in medical practice is likely to be revolutionary. Although we have already seen much promise in the application of pharmacogenomics, especially in cancer therapy, it may be safe to say the best is yet to come.

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Direct-to-Consumer Genetic Testing: Profile of 23andMe

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Since the advent of genetic biotechnology, the race to decode the human genome has progressed at an unprecedented pace. From the development of the polymerase chain reaction in the 1980s to the completion of the Human Genome Project in 2003, scientists have made huge leaps in the quest to better understand the significance of our genetic code.[1,2] Indeed, the information in our genome is becoming increasingly applicable to clinical conditions, causing debate over whether individuals should be able to readily access their genetic information without guidance from physicians. Multiple personal genomics companies offering direct to consumer (DTC) genetic testing have cropped up to capitalize on rising public interest, one of the first and most well-known being the California-based company 23andMe.

Founded in 2006, 23andMe has now arguably become the most widely used DTC genetic testing service.[3] For a fee of $299 USD, a Personal Genome Service kit will be delivered to the consumer's door.[4] The consumer simply has to spit into the sample collection tube provided and send the saliva sample back to 23andMe for testing in a private lab.[4] Testing detects single nucleotide polymorphisms (SNPs) associated with various conditions, and test results are accessible online within three weeks.[4,5] Personal results indicate disease risk and carrier status for 244 conditions, and are also used in the company's own research into the relationship between SNPs and genetic conditions, which is communicated quite clearly on the 23andMe website.[6,7]

Controversy arises, however, when considering how the consumers will interpret their test results. 23andMe does not offer genetic counseling, and the task of distinguishing between significant risks and negligible risks is not always simple.[8] Questions have also been raised over how informative certain results will be. While there may be correlations between certain genetic presentations and clinical outcomes, the multifactorial nature of many diseases may cause genetic results to be misleading and ambiguous.[8,9] Without adequate counseling and informed consent, consumers may also be unaware of, or ill-prepared for, the potential psychological consequences of knowing one's genetic predispositions.[8,9] Consumers may openly share their results with family members who share genetic information without first appreciating that not everyone may want to know his or her own disease susceptibility, which could potentially impart negative psychological effects on others. Many of these issues can be addressed with proper physician involvement and input, which are largely absent from most DTC genetic testing services.

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Despite the opposition of many members of the medical community to DTC genetic testing, public interest in accessibility to one's own genetic information is propelling the industry forward. In 2008, the state of California initially ordered the company to cease operations, stating that physician involvement was required in all genetic tests.[10,11] Four months later, the

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