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IP Policy Forum: Implications of Genomics Advances for Drug Discovery, Clinical Therapies, & Rare Disease Research

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IMPLICATIONS OF GENOMICS ADVANCES FOR DRUG DISCOVERY, CLINICAL THERAPIES, & RARE DISEASE RESEARCH

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The burgeoning field of genomics offers immense promise for the transformational power of personalized medicine. Genomics is the study of the full complement of DNA in an individual cell or organism. Personalized medicine is the customization of health care therapies to the individual patient. By sequencing the genome (DNA) of an individual, one can unlock the secrets of genetic causes of rare diseases, customize therapies for specific cancer types, and identify predispositions for complex diseases.[9] The ability to sequence the entirety of an individual's genome, and to analyze and annotate it have improved exponentially over the last few years, to the point that it is conceivable, and perhaps inevitable, that anyone who wants to have their genome sequenced will be able to do so for a relatively nominal fee within the next few years. The confluence of rapid, high-capacity sequencing instruments; new bioinformatic tools; a rapidly growing catalogue of disease mutations and allelic variations; and powerful computational resources and data storage availability will enable disruptive innovation that will make genomics an integral part of health care and wellness strategies in our lifetimes. The transformative potential of genomics in personalized medicine is particularly meaningful to us in Milwaukee, as much of the groundbreaking work has been performed at and with the support of the Medical College of Wisconsin and Children's Hospital of Wisconsin.

9. Howard J. Jacob, et al., *Genomics in Clinical Practice: Lessons from the Front Lines*, 5(194) SCIENCE TRANSLATIONAL MEDICINE 194cm5 (2013).

Genomics will revolutionize drug discovery in at least four ways. First, by identifying the causes of rare diseases, scientists and clinicians will create clues about heretofore unknown and possibly unsuspected functions of genes. These clues will lead to new mechanistic insights that will create novel "druggable" targets. The druggable targets should be amenable to high throughput screening, *in silico* analyses and other drug discovery methodologies, which in turn, will lead to innovative therapies.

Second, clinicians will be able to optimize drug therapy for specific syndromes for each patient based on their genomic sequences, by choosing the drugs that are most likely to work, and by avoiding those that can cause serious side effects. It is now well known that a significant percentage of the population does not obtain a therapeutic benefit from clopidogrel,[10] a potent (and expensive) anti-platelet agent used in the prevention of heart attacks and strokes. Clopidogrel is a pro-drug that requires a certain enzyme (CYP2C19) to become active. Genetic mutations of that enzyme impair the metabolism of clopidogrel, rendering it ineffective. With regard to side effects, angiotensin-converting enzyme inhibitors (ACEI) are highly effective antihypertensive drugs. But, ACEI can cause a dry cough in a significant number of patients that can lead to non-compliance; ACEI also can cause life-threatening angioedema. Both of these side effects have been linked to or are suspected to be associated with specific genetic variations.

Third, by knowing genetic predispositions of each patient for various "preventable" diseases, the patient could modify risk factors and behaviors (diet, smoking, exercise). Those risk factors could be ameliorated directly by drug therapies, or perhaps indirectly with the assistance of new types of medicines or nutraceuticals that would encourage or enhance the effects of healthy behaviors. Those medicines and nutraceuticals would be amenable to drug discovery.

Fourth, a better understanding of the genetic bases of unwanted side effects of drugs could lead to improved agents with intact therapeutic profiles and reduced side effects through rational drug design or brute force screening methods.

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10. Simon Tabassome, et al., *Genetic determinants of response to clopidogrel and cardiovascular events*, 360(4) N. ENGL. J. MED. 363–75 (2009).