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Keynote Report:

The role of genomics in medicine —past, present and future*

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The fundamental idea that responses to environmental factors or treatments is to be found in our individual differences, the underlying concept of “genomic medicine”, is rooted in antiquity and based on millennia of simple observation. Simply put, the objective of genomic medicine is to determine the genetic bases of those differences in response to environmental agents, including medications, and differences that may predispose to the development of common and potentially personally devastating and societally expensive disorders, and to use them in populations to thwart adverse response, increase the frequency of beneficial response, and intervene to prevent or delay onset of disease.

The medical implication of individual variation was well known more than a century ago and perhaps, best annotated by Garrod in the early days of the 20th century. Since then the idea that these individual differences had a genetic basis and thus were likely shared in populations with similar origins has grown so that testing a few individuals for variants could provide ways to identify individuals within that group to target for intervention.

In a sense, the easy work of genomic medicine has been completed—the near-finished complete draft of the human genome sequence, the development of tools that allow high throughput targeted resequencing of the genomes of multiple individuals, the identification of some major alleles that predispose to development of identifiable genetic disorders and of other that increase the background risk for the development of more common conditions, the development of sensitive and convenient gene expression arrays, and the refinement of computational tools to use them. But, those are the easy steps.

And they have led to some notable, though relatively small scale, success stories. These include identification of individuals at risk for adverse reaction to chemotherapeutic drugs on the basis of variants in processing enzymes, the prediction of response of malignancies to drugs and of their propensity for metastasis on the basis of expression profiling, and the development of drugs based on detailed knowledge of receptor structure.

There are several areas of new knowledge that will have to be developed to create a reality of genomic medicine. These include the characterization of genomic variation among individuals in the target populations (and each separate population will probably have to be studied anew), the identification

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of the clinically significant variants in each group, the assessment of the extent to which intervention could change predicted outcome—taking into account other changes in environmental exposure and behaviors, and the development of an understanding of the costs of these processes for the society and weighing them against other societal needs.

In societies in which pandemic disorders are the result of behavioral and societal excesses (obesity, diabetes, and the like) or scarcities (starvation, endemic infection) genomic medicine as a health strategy may come second to other public health interventions in efficacy.



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