Personalized medicine: “Tyranny of the gene”

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Dr Priya Hays, Ph.D., CEO/Science Writer at Hays Documentation Specialists, LLC, responds to “Tyranny of the Gene.” Is personalized medicine a threat to public health? Not really, but yes, it’s an argument for price controls and perhaps more regulations; we hear

Tyranny of the Gene: Personalized Medicine’s Threat to Public Health, written by James Tabery and published by Alfred Knopf Publishers, was released in August 2023 and was featured in a New York Times Op-Ed. Tyranny of the Gene is a historical account of the origins and development of genomic and personalized medicine, shedding light on examples of unsavory scientific and medical experimentation during its early period intersecting with the eugenics movement and research behind the birth of pharmacogenomics.

Tabery delves into its growth as a result of capitalist incentives for pursuing profits in industry rather than the goal of achieving effective patient care, which is the most often cited reason for seeking its implementation among its supporters. The nature-nurture debate takes a central stage in this book, creating a dichotomy that public health is environment-based (or nurture) and personalized medicine is the gene (or based on genetic predisposition or nature), with genetic reductionism playing a pivotal role in its rise, according to Tabery.

Tabery also chronicles how low-tech public health initiatives in determining environmental effects on children’s health were sacrificed for genome- oriented studies in the early twenty-first century, arguing that “genome imperialism” has overshadowed efforts to address our unsafe and unhealthy environments, leading to racial health disparities.

Transformation of personalized medicine

Personalized medicine, though, remains epistemologically neutral to the aims of public health, especially in precision oncology, which I will concentrate on, and does not pose obstacles to public health initiatives. Consider the PRECEDE study, Pancreatic Cancer Early Detection Consortium, designed to prevent pancreatic cancer or detect it earlier, and the development of more effective therapies to improve survival outcomes, a public health initiative based on personalized medicine for screening and early diagnosis of pancreatic cancer, a disease with poor prognosis. The PRECEDE study uses technologies made possible by precision medicine, such as biomarker testing and large data collection. (1)

New scientific and clinical methodological approaches have emerged with the transformation of personalized medicine clinical care. The standard methodology was to conduct a clinical trial, determine the clinical efficacy of the agents and associated side effects, and administer the appropriate treatment and dosage for the disease or illness. Now, gene testing panels and whole exome and genome sequencing are conducted for patients, followed by the administration of suitable targets for druggable mutations in disease after establishing clinical efficacy through clinical trial data assisted by the prognostic and predictive capabilities of companion diagnostics.

The transformation of this particular bench to bedside or translational medicine model did not happen overnight. It took the coordinated efforts of well-meaning physician- scientists, researchers, drug developers, and biotechnology companies along with a handful of regulators and the dissemination of their efforts, particularly in oncology journals and the publications of medical societies such as the Journal of the American Medical Association, American Society of Clinical Oncology and Society of Immunotherapy of Cancer, to name a few, over at least the prior twenty years, stemming from the sequencing of the human genome leading to a biological understanding of the importance of individual molecular variability.

The discovery and progression of immunotherapeutic agents by seminal work performed at academic medical centers and government agencies have rapidly changed the face of personalized therapy and healthcare.

Tumor types

Most tumor types, such as the one Tabery's father passed away from, non-small cell lung cancer, have been affected by this medicine paradigm. The long list of tumor types now considered amenable to targeted therapy and immunotherapeutic approaches is long, including the most prevalent, breast cancer, lung cancer, melanoma, colorectal cancer, prostate cells, B cell, and myeloid malignancies.

Plus, tumor types are growing with each discovery of new mutations, leading to the development of genomic testing panels and biomarkers such as tumor mutational burden and PD-L1, novel ways of characterizing tumor heterogeneity and affecting the tumor microenvironment, and the astounding pace in the development of cancer immunotherapies, from immune checkpoint inhibitors, adoptive cellular therapies, bispecific antibodies, and antibody-drug conjugates.

Next-generation therapies

Researchers are continuing further with the strong impact of these advances. With tumor resistance and non- response observed, next-generation therapies for solid tumors and hematological malignancies emerged continually, each defined by its own specific mechanism of action from their precursors that have even better clinical outcomes and response with the goal of achieving better tolerability and fewer adverse events, and thereby improving quality of life.

While anti-CTLA-4 and anti-PD-1 inhibitors became standard of care, agents such as the LAG-3, TIGIT, and TIM-3 antibodies were developed with less non-responders. When autologous chimeric antigen receptor T-cell therapies showed remarkable efficacy and prognosis for diffuse large cell B- cell lymphoma, a cancer affecting children, becoming a formidable component of cancer care, the prospect of allogeneic stem cell therapies weas soon articulated, envisioning a less laborious process of administering CAR T-cell therapies. [2,3]

Patients' lives are being drastically changed, with some exhibiting remarkable results, overcoming the challenges of a persistent illness that spreads in many cases. Breast cancer and melanoma are case examples. According to the data released within the last twenty years, objective response and survival rates of personalized oncology drugs increased considerably in clinical trials enrolling these patients. [4-8]

Prevention and early detection in personalized medicine

Topics such as prevention and early detection are being considered avidly in the context of personalized medicine. Early detection is of profound importance in personalized medicine- initiated care, since it has been shown, as an example, through evidence that when cancer cells are detected at early stages (Stage I and II) through liquid biopsy, treatment is more efficacious with demonstrably improved clinical outcomes and greater odds of remission when compared to detection at later stages (Stage III and Stage IV).

Healthcare disparities among minority populations are receiving increased attention from the medical community due to personalized medicine. Latinx and Black Americans continue to be underrepresented in clinical trial participation. There is now the developing notion of "implicit bias" in providers, leading to preferential treatment in patient care based on ethnicity and calling for more equitable care for a diverse patient population. Personalized medicine is not hampering these efforts and may, in fact, be playing a positive role.

Financial toxicities stemming from expensive precision medicine drugs are burdening patients, as Tabery argues. For example, cancer is considered the primary reason patients file for bankruptcy due to exorbitant medical bills. Even as clinical trials are being streamlined to mitigate drug development costs, the total cost of care is out of reach for the average income. In short, our healthcare system needs to be "healthy" as much as the patient, and there is certainly a need for price controls through health economics/policy analysis, rather than stemming the gains of personalized medicine.

A balanced perspective for personalized medicine

There are ways to go about implementing healthy advances in personalized medicine within the present healthcare system and economy:

- Educating the public about its positive aspects, underscoring highlights such as polygenic genomic variation and epigenomics and presenting a balanced view of the challenges it faces, ensuring its clinical and scientific value to society, along with the necessity of addressing social and environmental determinants of health for diseases such as diabetes and asthma, particularly for vulnerable and minority populations.
- More oversight from government bodies to regulate the potential physical and environmental harms of medications and technologies and evolving from free market-libertarian principles.
- Pharma and academic medical centers play an active role in enrolling underrepresented populations in clinical trials, which has already, to some extent, taken place.
- Contextualize the analysis of personalized/precision medicine with the objective presentation of data and model mechanisms of action.
- Emphasize the growth of gene panels rather than only documenting the development of genome-wide association studies (which had equivocal success and identified causal variants for a small percentage of the population), and next-generation sequencing and present the many success stories along with cases that have not met with robust clinical outcomes.

Henceforth, there should be synergy between public health and personalized medicine; however, there is very little inherently about personalized medicine, as presented in Tabery's account, which would prevent that.

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