Translational Medicine in the Era of Health Care Reform

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Global health care delivery is in an unsustainable economic pandemic. In the United States alone, costs are estimated at $2.5 trillion, dramatically escalating from $253 billion just 2 decades ago.[1] Although all elements of the health care system have experienced exponential inflation, the emerging crisis is exemplified by the impact on pharmacotherapy, commonly recognized as the most cost-effective component of the disease management armamentarium. Drug costs are rapidly escalating, and therapies that cost a few hundred dollars 2 decades ago have been replaced with new drugs in excess of hundreds of thousands of dollars.[2,3] This challenge is compounded by a coordinate burden of the drug development process, in which success rates have significantly declined to about 5%, with development costs exceeding $2 billion for each marketed drug, limiting the availability of first-in-class therapeutic agents in medical practice.[1–3]

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Beyond established pharmacotherapy, the marketplace has been flooded with diagnostic and therapeutic products of uncertain health care impact offered to patients through direct-to-consumer advertising that represent a substantial drain on the medical commons.[4] This confluence of crises in health care in the context of the aging population, associated with an increased demand on these systems, underscores the opportunity offered by translational medicine, whose dynamic evolution across the entire spectrum—from discovery and development through evidence-based assessment of diagnostic and therapeutic strategies—provides solutions critical for optimum health care resource allocation and drug and diagnostic development and application.[5]

How Translational Medicine Is Unique

Translational medicine integrates management paradigms across the spectrum of disease pathophysiology.[6] As the science matures, the empiricism of medical practice is replaced by mechanism-based targeted diagnostics and therapeutics. Information synthesized from insights into molecular circuits and pathways underlying disease provides a foundation for longitudinal health and, when appropriate, guides therapeutic management of incipient disease.[7] This escalating revolution in the products of discovery science has transformed our perspective of human wellness, offering an attractive context for translational medicine as the integrated science of discovery, development, and application, and for the translational medicine practitioner as a pivotal link between laboratory, patients, and populations.[8]

Innovations in translational medicine have driven the discovery of therapeutic solutions across the continuum of prevention, diagnosis, prognosis, prediction, and cure in pursuit of individualized health care management. Reciprocally, translational medicine has become the vehicle for clinical application of the new biology and the translation of molecular insights into practice.[7] In that context, emerging molecular technologies have provided tools to define processes underlying disease initiation and progression, identifying novel pathways for diagnostic and therapeutic intervention.[9] Translational medicine has been pivotal in identifying quantifiable molecular diagnostics predicting clinical outcomes, therapeutic responses, and idiosyncratic adverse reactions.[7,9] Collectively, it offers a perspective on disease pathophysiology, defining the tempo of progression of mechanisms of disease from risk susceptibility to overt illness.[7] These mechanistic insights offer a previously unrecognized opportunity to identify and interrupt nascent corruption of normal physiological processes prior to the establishment of indelible pathological mechanisms encompassing irreversible morbidity. The science and enabling technologies undergirding translational medicine increasingly drive drug and diagnostic development, providing a profusion of new tools available to clinicians for patient management.[6]

The Potential to Transform All Aspects of Health Care

Management of new knowledge through the electronic medical record offers the opportunity for an integrated personalized clinical decision support system.[10] Translational medicine is particularly well situated to explore platforms tailored to individual genetic profiles aimed at ultimately improving diagnostic and therapeutic specificity while minimizing adverse outcomes.[9,11] Personalization has the potential to transform all aspects of health care and increasingly is becoming a part of daily practice.[10,12] Genetic stratification of patients offers previously unanticipated opportunities for success in pharmaceutical and biotechnology development. Gene–environment interactions contributing to variability in therapeutic responsiveness provide unique insights into interindividual variability in drug efficacy and toxicity. Further, integration of disease mechanisms at the level of genes and molecules enables optimum integration of individual patients, personalized diagnostics, and therapeutic agents to truly individualize clinical care. New models of care are being developed to leverage the advances in regenerative translational medicine to bridge the spectrum of disease management from palliation to cure.[13] Collectively, translational medicine and the associated identification of genetic and molecular circuits offers fully integrated personalized health care solutions that

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redefine therapy and prevention at the level of individuals and populations.[6,9,11]

Scientific insights into molecular mechanisms have transformed opportunities for patient management and clinical care beyond individual patients to global populations.[9,10] It is noteworthy, however, that this evolution has advanced disproportionately across the different elements of the translational medicine continuum.[14] There have been dramatic advances in T1 translation encompassing the discovery of novel mechanisms underlying health and disease, fueled by the enabling "omic" technologies. In striking contrast, there has been a paucity of progress in T2 translation, moving these discoveries into development to acquire the evidence base required for clinical application. There is also a shortage of T3 translation, in which the evidence base supports incorporation of the new transformative technology into clinical practice guidelines. Moreover, there is a near absence of T4 translation defining the uptake of the new technology into practice and its impact on individual patient outcomes, population health, and health care expenditures. It is only through embracing the full spectrum of translational medicine encompassing T1–T4 investigation that the value of the new biology to improve patient care and health outcomes across populations can be realized. This revolution in health care only can be achieved in the context of appropriate societal policies that equitably distribute evidence-based high value technology to all members.[14] Intuitively, there is a societal expectation that the individualization of medicine will provide an integrated solution to the accelerating global crisis in health care. That expectation is, in part, anchored in the principles guiding evidence-based evaluation of technology and its added value to individual patients, populations, the health care system, and society.

In that context, the outputs of translational medicine have the potential to contribute to solving, rather than exacerbating, the global health care crisis. Molecular profiles stratify individuals, defining technology platforms that identify patients at risk for disease and permit preventive interventions associated with economic benefits including reduced disease, improved quality of life, and prolonged productivity. Similarly, disease stratification permits optimization of populations participating in pivotal clinical trials, improving the success of drug development and maximizing return on investment.[11] Genotyping and phenotyping identify individual patients at greatest risk for adverse drug events to optimize safety and reduce comorbidities and their associated societal costs. Moreover, predictive biomarkers identify patients most responsive to specific therapies, targeting limited economic resources where they will provide maximum benefit.[11] These previously unrecognized abilities optimize diagnostics and therapeutics across populations with genetic and environmental variabilities, and improve success rates in drug discovery and development and return on investment in the pharmaceutical and biotechnology industries. These abilities also maximize therapeutic efficacy and reduce idiosyncratic drug reactions, improving drug safety.[7]

Translational Medicine: An Economic Hindrance?

Although these considerations suggest that the societal benefits accruing from the new biology are self-evident, there is potential for translational medicine to add economic stress to an already overburdened health care system.[14] In the context of the emergent position of molecular techniques in the management of patients, with their sensitivity for detecting disease and revising prognoses, it is the responsibility of drug and diagnostic developers, health care providers, regulators, and insurers to consider whether the evidence base supports the availability of clinical and economic resources for the application of the products of translational medicine to individuals and populations.[12] Standing on the verge of this revolution in personalized patient management at every level, including risk assessment, prevention, diagnosis, and cure, through application of cutting-edge technology and, at the same time, contemplating the global crises in health care, it is incumbent on us to consider the societal benefits and risks of the new biology, whether there is an adequate evidence base for its adoption into clinical practice, and whether we have the social, political, and regulatory will to manage its application with fiscal responsibility and equity.[12]

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