The Roadmap to Personalized Medicine

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Individualized medicine is an emerging concept instrumental to realizing the clinical value of advances in the new biology, and it is driving translation of discovery to patient-specific practice. Modern biotechnology provides an enabling platform to customize patient-specific strategies based on individual genetic makeup to predict, prevent, diagnose, and treat subtypes of disease beyond the traditional "one-size-fits-all" approach.[1] This novel concept is brought into specific relief considering that there are 25,000 genes in humans and the information encoded therein is exponentially compounded by >100,000 splice variants of messenger RNA. Further, there are 15 million loci along the genome where a single base can differ between individuals or populations. Three million of these single-nucleotide polymorphisms have been identified, generating the HapMap which has been used in genome-wide association studies to map polygenic diseases.[2] The enormity of molecular diversity is further amplified by systems-wide epigenetic and post-translational modifications, underscoring the challenge of individualization through diagnostic and therapeutic targeting. This biological diversity inherent in individuals and populations offers unprecedented opportunities to tailor prevention and treatment, while minimizing off-target adverse events, ultimately transforming health care delivery at the bedside.[3]

Individualized medicine draws from all life sciences, providing a unifying platform through otherwise disparate medical specialties. Its value is rooted in its comprehensive approach, where the coevolution of molecular diagnostics and targeted therapeutics reflects advances in discovery science, continuously directed by feedback from regulatory and utilization paradigms.[4] In this context, the goal of personalized medicine is to expand the achievable metrics of clinical care beyond palliation by ensuring disease prediction, prevention, and cure.[5] Individualized medicine contributes to the continuous transformation of health care delivery on a national and global basis.[1] It offers unique opportunities for estimating disease risk across broad populations. It exemplifies the continuous evolution of prevention strategies, including vaccination of global populations for targeted eradication of diseases. Pharmacotherapy, as the most cost-effective management tool in the clinical armamentarium, will particularly benefit from advances in individualized medicine, enhancing the cost-effectiveness value by prognostic and predictive stratification of patient populations, targeting disease processes, and avoiding life-threatening adverse events. The shift from palliation to curation with the revolution in regenerative medicine and therapeutic repair offered by individualized medicine has the potential to transform the efficiency of disease resolution, shortening hospital stays and decreasing health care expenditures.

The ongoing transformation in technology and discovery has produced a marked evolution along the entire downstream continuum of diagnostic and therapeutic development toward realizing the promise and potential of the new biology in individualized and population medicine. Diagnostic and therapeutic advances have been driven by the parallel development of high-throughput technologies and conceptual advances in molecular mechanisms underlying disease and yielding targets of increasing complexity that address individualization of medical management.[6] Indeed, beyond specific groups of biomolecules, the entire transcriptome or proteome can be assessed, distinguishing diseased and normal tissues or disease categories with different risk profiles. Technological advances in discovery science have entrained novel paradigms addressing diagnostic and therapeutic validation, clinical qualification, and application. For example, for molecular biomarkers of disease, these considerations raise the need for regulatory oversight of analytic validation to define performance metrics—including reproducibility, sensitivity, and precision—and assure clinical qualification, in order to systematically transition from discovery to clinical care.[6] Additionally, quantitative and qualitative relationships between biomarkers and disease management will require rigorous clinical qualification, with evidence linking a biomarker with biological and clinical endpoints. Relationships describing the clinical utility of biomarkers will require assessment in prospective randomized clinical trials and subsequent validation in follow-up trials.[6] Integration of molecular diagnostics and targeted therapeutics into clinical paradigms for patient management will require dramatic changes across the continuum of discovery, development, regulation, and utilization, requiring collaboration across communities of practice.[7-10] Realizing this envisioned future will also require collaboration among stakeholders involved in the development, application, and regulation of molecular medicine. As progress unfolds, the evolution of an unprecedented personal information stream will mandate the establishment of rigorous bioethical guidelines to direct utilization in patient management.[11] Taken together, these considerations highlight molecular medicine as the path forward from the current curative model of patient care to preemptive prognostic and predictive medicine.[12]

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