CCBIO Opinion

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Precision Medicine - Lost in Translation?

Inter-individual and inter-cellular molecular diversity is associated with specific disease processes as well as with diverse life outcomes. During the last two decades, the attention of biomedical, translational and clinical research has converged towards the study of such molecular heterogeneity, in an attempt to translate precise biological understanding into meaningful clinical applications. Substantial accomplishments attributed to this approach have resulted in the development of medical strategies characterized by incorporation of molecular characteristics in disease categorization, prognostication, clinical decision-making and therapeutic development. The traction of these strategies has been enforced by rapid technological advancements, as well as broad financial and political support. Novel relationships between stakeholders have developed and matured, resulting in the emergence of a co-produced imaginary; precision medicine. This imaginary is not confined by clinical applicability but is a compound concept built on ambitions and visions of what can be achieved through increased precision in medical care; visions of a future with far less disease, suffering and death. Founded on these promises, techno-scientific optimism and assumptions of benefit, a profound transformation of health care practices, health care delivery systems, knowledge generation, policy and regulatory strategies have been set in motion, gradually translating concept to reality.

Importantly, the imaginary of precision medicine serves a democratic and ethically grounded goal; improving life quality and population health outcomes. The utility, validity and legitimacy of precision medicine should therefore be evaluated and deliberated upon in this explicit context. Although observational and experimental experience suggests that precise medical strategies are feasible and sometimes efficient, the political as well as scientific discourse of precision medicine is predominantly built on visions rather than realizations. This is accentuated by estimates suggesting that less than 5% of the American cancer patient population currently benefit from precision medicine (Marquart, Chen et al. 2018), and that most recent European market approved oncologic agents either fail to display, or demonstrate only marginal improvements in survival time or quality of life (Davis, Naci et al. 2017).

It is appealing to attribute these sobering results to lack of knowledge, and shortage of clinical tools and targeted agents. It is, however, also possible that the expectations of precision medicine fundamentally fall short due to its lack of true inherent potential. The investigational objectives of CCBIO exceed the traditional molecular emphasis of precision medicine and focus on an expanding biological understanding of cancer cells' contextual relationships. CCBIO researchers have repeatedly demonstrated that interactions amongst cells and between cells and their physical and biochemical microenvironment influence emerging cellular properties and shape disease trajectories. This dynamic interplay has further been shown to impact both therapeutic responses and disease outcome. Cancer, as portrayed by CCBIO researchers, is an evolving relational process; profoundly imprecise in descriptive and functional terms. With this in mind, the pressing question is whether precision medicine can ever be precise enough to truly provide benefit in a public health perspective, technical and financial constrains set a side.

As researchers and experimentalists, our mandate is to generate and disseminate knowledge to inform democratic processes. Repercussions of the dissonance between investments, expectations and the current reality of precision medicine are materializing, and perhaps righteously negatively influencing the legitimacy of both precision medicine and policy makers. Our constructive contribution in this discourse should include management of expectations and disclosure of limitations and uncertainty. We cannot know if precision medicine will provide sizable benefits on a population level in comparison to alternatives. We do however know, with great confidence, that precision medicine will not solve the problem of suffering and mortality. When overpromises are made, it is in our interest to modify the "great expectations"; to protect the legitimacy of our work and our investments. ••

Davis, C., H. Naci, E. Gurpinar, E. Poplawska, A. Pinto and A. Aggarwal (2017). "Availability of evidence of benefits on overall survival and quality of life of cancer drugs approved by European Medicines Agency: retrospective cohort study of drug approvals 2009-13." BMJ 359: j4530. Marquart, J., E. Y. Chen and V. Prasad (2018). "Moving Precision Oncology Forward Amid Myths and Misconceptions-Reply." JAMA Oncol 4(12): 1790.