

RESEARCH HIGHLIGHT

Systems medicine and the public's health

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Abstract

Innovative 'systems' approaches to biomedical research offer substantial promise for advancing knowledge and improving health care, as outlined by Bousquet *et al.* in this issue. However, they are unlikely to improve population health without concurrent efforts to address environmental and social contributors to health, including conditions such as poverty, substandard housing, and restricted access to employment and education. Biomedical researchers have a responsibility to promote realistic expectations for systems or 'P4' medicine, and to join others in calling for broad efforts to promote equitable access to health care and social conditions that promote well-being.

'P4' medicine

Systems or 'P4' medicine offers a grand vision for achieving better population health. The four Ps - predictive, preventive, personalized and participatory - invoke a patient-centered approach that prioritizes health promotion over disease treatment. In this issue of *Genome Medicine*, Bousquet and co-authors [1] suggest that this approach will be especially suitable for non-communicable diseases (NCDs), conditions such as heart disease, cancer and diabetes that represent large and growing public health burdens. Their optimism is based on an increasing array of molecular tools to investigate biological systems at an unprecedented level of precision. The authors call for population-based research aimed at understanding how NCDs 'cluster at the genetic, molecular (and) mechanistic levels and are affected by environmental and social factors'; the anticipated result is a redesigned healthcare system that identifies early disease and delivers beneficial, cost-effective interventions. The potential benefits of this research paradigm are impressive - but closer inspection suggests that caution is in order.

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As Bousquet and colleagues observe, most common diseases have a complex etiology that includes host, environmental and social determinants, acting across the lifespan. In particular, social conditions such as poverty, substandard housing and restricted access to employment and education are strongly associated with negative health outcomes [2-4]. How adverse social conditions contribute to disease remains poorly understood; if systems biology can elucidate this relationship, it might lead to welcome new strategies for prevention or early treatment. Such developments would represent an important advance. However, P4 medicine cannot solve the root problem: the need for political and public health action to improve the life chances of disadvantaged people [2]. In this context, a realistic assessment of the prospects for systems biology is sorely needed.

Weighing the contributions of P4 medicine

A central component of the P4 medicine vision is that an array of new biomarkers will identify diseases at early, treatable stages, enabling effective prevention of morbidity and mortality. This approach is intuitively appealing. Early detection already offers important life-saving opportunities - for example, mammography and phenylketonuria screening. But early detection has its failures as well. Newborn screening for neuroblastoma, for example, increased detection rates but had no impact on disease mortality [5] - and led to iatrogenic harm (that is, injury through medical treatment): screening missed some severe cases, and found others whose relatively benign course did not require early treatment [5]. Similarly, the use of the prostate-specific antigen test for early detection of prostate cancer is associated with limited mortality benefit and significant harm, including impotence and incontinence, due to overtreatment of latent cancers [6,7].

The reason for these difficulties is not hard to find: screening is complicated by false-positive/false-negative results (screening may suggest a condition that is not present, or fail to identify a condition that is); lead time bias (screening may identify a disease early without prolonging survival); length bias (screening may disproportionately identify less-aggressive, slower-progressing disease); and overdiagnosis (identification of early disease

in people whose course would be benign if left untreated) [6]. These problems, and in particular limited predictive value and overdiagnosis, are likely outcomes for biomarkers associated with NCDs because of the variable course of these conditions and the important contribution of social and lifestyle factors to outcome [2,3]. Undoubtedly, systems biology will help to refine screening protocols, and some P4 biomarkers will have sufficient predictive value to improve care, but past screening experience tells us that none will be fully error free [6].

As with biomarkers, systems biology offers promise for drug discovery [1]. However, drug development is notoriously difficult: predictive models are theoretical and do not always withstand testing; animal models are an inexact facsimile of human biology; and targeting one part of a given pathway may have unforeseen effects elsewhere. Systems biology is likely to make important contributions, but progress will still be slow because a large complement of targeted therapeutics will be needed for substantive healthcare improvement.

The prospects are less clear for a P4 contribution to health behaviors. Although some effective strategies for improving health behaviors are emerging [8], the role of biomarker-based behavioral change appears limited. DNA-based risk prediction, for example, appears to have little or no effect on health behaviors [9] - and social conditions represent formidable barriers. A patient who faces difficulty housing or feeding her children is unlikely to spend resources addressing a possible future health risk. Likewise, using P4 profiling to encourage intake of green, leafy vegetables is of limited value for a patient living on the northern tundra or in an inner-city neighborhood with no gardens or grocery stores. Solving these problems will require efforts beyond the realms of biomedical research and health care.

P4 medicine and research participation

Achieving the benefits of systems biology will require substantial research participation and investment in research infrastructure. Bousquet and colleagues propose that individuals have a 'societal responsibility to make their anonymized data available to appropriate scientists and physicians' in order to accomplish the research necessary for P4 medicine. Certainly the inclusion of diverse populations will be necessary to ensure that the benefits of research are broadly relevant [10].

In the absence of the political will to address poverty and other social conditions associated with poor health outcomes, many people will continue to have limited access to effective health care and therefore little motivation to participate in research aimed at improving it. The argument that they have an obligation to do so is difficult to justify when there is no assurance that they - or their descendants - will reap the benefits. Accordingly,

Bousquet and colleagues call for increased efforts to address the social determinants of health, arguing that 'P4 medicine development should be a global aim and not a privilege of 'rich' countries.' Beyond moral exhortation, biomedical researchers face the serious question of how to engage with this dilemma.

The way forward

What can researchers do to encourage increased research participation based on reasonable expectations? And how can they contribute to broader efforts to improve health equity? An important starting point is to avoid suggesting that P4 medicine will provide the much-wished-for magic bullet. Policy makers would undoubtedly welcome a technological fix to population health. Researchers must avoid overpromising, and instead should counsel policy makers that efforts to improve social conditions have a greater potential to enhance population health than even the most optimistic projections for P4 medicine.

Systems biology is poised to provide a wealth of new knowledge about human health and disease. Opportunities for improving health care will emerge, and these are reason enough to celebrate the systems biology approach - but they will not solve the tough social issues that lie at the center of population health challenges. Bousquet and colleagues have it right when they link P4 medicine to a call to address social inequities. In doing so, they acknowledge the limitations of biomedical research and the importance of thinking beyond biological systems to the political, psychological, socio-cultural and economic realities that shape them.

Abbreviations

NCD, non-communicable disease.

Competing interests

The authors declare that they have no competing interests.

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References

1. Bousquet J, Anto JM, Sterk PJ, Adcock IM, Chung KF, Roca J, Agusti A, Brightling C, Cambron-Thomsen A, Cesario A, Abdelhak S, Antonarakis SE, Avignon A, Ballabio A, Baraldi E, Baranov A, Bieber T, Bockaert J, Brahmachari S, Brambilla C, Bringer J, Dauzat M, Ernberg I, Fabbri L, Froguel P, Galas D, Gojobori T, Hunter P, Jorgensen C, Kaufmann F, et al.: **Systems medicine and integrated care to combat chronic non-communicable diseases.** *Genome Med* 2011, 3:43
2. World Health Organization Commission on Social Determinants of Health: *Closing the Gap in a Generation: Health Equity Through Action on the Social Determinants of Health.* Geneva: World Health Organization; 2008. [http://whqlibdoc.who.int/hq/2008/WHO_IER_CSDH_08.1_eng.pdf]
3. Lewis SJ, Leeder SR: **Why health reform?** *Med J Aust* 2009, 191:270-272.
4. Farley TA: **Reforming health care or reforming health?** *Am J Public Health* 2009, 99:588-990.
5. Woods WG, Gao RN, Shuster JJ, Robison LL, Bernstein M, Weitzman S, Bunin G, Levy I, Brossard J, Dougherty G, Tuchman M, Lemieux B: **Screening of infants and mortality due to neuroblastoma.** *N Engl J Med* 2002, 346:1041-1046.
6. Welch HG, Schwartz LM, Woloshin S: *Overdiagnosis: Making People Sick in the Pursuit of Health.* Boston, MA: Beacon Press; 2011.

7. Ilic D, O'Connor D, Green S, Wilt TJ: **Screening for prostate cancer: an updated Cochrane systematic review.** *BJU Int* 2011, **107**:882-891.
8. Spahn JM, Reeves RS, Keim KS, Laquatra I, Kellogg M, Jortberg B, Clark NA: State of the evidence regarding behavior change theories and strategies in nutrition counseling to facilitate health and food behavior change. *J Am Diet Assoc* 2010, **110**:879-891.
9. Marteau TM, French DP, Griffin SJ, Prevost AT, Sutton S, Watkinson C, Attwood S, Hollands GJ: **Effects of communicating DNA-based disease risk estimates on risk-reducing behaviours.** *Cochrane Database Syst Rev* 2010, **10**:CD007275.
10. Fullerton SM: **The input-output problem: whose DNA do we study, and why does it matter?** In *Achieving Justice in Genomic Translation: Rethinking the Pathway to Benefit*. Edited by Burke W, Edwards KA, Goering S, Holland S, Trinidad SB. New York: Oxford University Press; 2011, p59-78.

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