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All the postgenomic world is a stage: the actors and narrators required for translating pharmacogenomics into public health

"A taxonomy of actors and dual-order narrators takes the concept of innovation systems to a new level of stringency and standards."

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Taking innovation from the clinic to the streets

The now decade-old postgenomic era is marked with stories of triumph and tribulation, hope and hype, and gradual, sometimes serendipitous, innovations in personalized medicine [1]. While governments have prioritized research and development (R&D) and moving discoveries from laboratory to innovation [2], innovations (especially those in the biotechnology sector) have often underwhelmed governments, investors and the public in terms of utility [101]. The postgenomic era now includes direct-to-consumer genomics and is moving into its second decade [3]. We suggest that the personalized medicine innovation system is highly fluid and in flux as a result of fiscal restraint, and old ways of understanding innovations' nature and predictability are undergoing transformation. Much of the western world is now locked in a straight-jacket of budgetary constriction; past calls for more R&D funding simply will not do as the fight for increasingly small resources intensifies and citizens resist the idea of greater taxation. New ways of conceptualizing innovation must take hold, embracing uncertain, contingent, discursive processes and questioning prior unchecked assumptions, values and constraints in the innovation system.

We propose a new taxonomy for the 'public health pharmacogenomics' innovation ecosystem [4,5], labeled 'actors' and 'narrators', which takes innovation out of the laboratory and into the 'streets', and examines the embedded interests and unchecked power structures impacting knowledge coproduction among the innovation actors.

Actors & narrators: a new taxonomy for innovation ecosystems

Innovations are now being understood, given their financial and societal significance, as engaged practices that move discursively in a knowledge ecosystem. While we certainly support the extant move toward 'opening up' the discussion on scientific design [6], there is a danger in succumbing to a false sense of assuredness that simply by bringing more people to the table, the innovation system will magically be more ethically just and socially robust. We cannot merely wish it so.

To avoid falling into the trap of tokenism or unidirectional political legitimacy (i.e., more is always better), research funding agencies invested in pharmacogenomics and traditional innovation actors, such as academic scientists, industry and governments, must remain cognizant that aggregating publics and creating more time and space for dialogue do not necessarily lead to innovation or to better innovation that is sustainable [7]. Multitudes of voices and opinions, brought together without a sound social theory, can be cacophonous, counterproductive and at risk for tokenism [8].

One of us (V Özdemir) has outlined a new taxonomy for understanding innovations and the attendant knowledge ecosystems as consisting of actors and narrators [9]. In this taxonomy, innovation actors – those who carry out core discovery and translational work, such as pharmacogenomic scientists – are situated at arm's length from first-order narrators, such as social scientists, lawyers, philosophers and bioethicists, who, armed with their own variable form of expertise, are acknowledged to play a critical role



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in exploring the ethical, legal and social implications of postgenomics research for individuals, families and communities. However, as with innovation actors, first-order narrators never come free of social interests or implications. In our proposed nested governance frame for knowledge-based innovations [9], first-order narrators are subject to engagement by experience-based second-order narrators, such as citizen scholars, knowledge endusers and traditionally marginalized groups, so as to prevent actors and first-order narrators from gaining excessive power that can be misused in the course of steering innovations. This dual ordering of narrators, as distinct from actors, is crucial for the additional reasons we explain below.

Listening to the sound of silence: toward a sociology of bioethics

We have long seen the emergence of different professionals, such as social scientists, bioethicists and philosophers, engaged in a narrator role in pharmacogenomics, but our taxonomy of knowledge coproduction noted above takes the actor–narrator dialectic to a greater level of accountability by underscoring that first-order narrators also have self-interests that ought to be made explicit for innovations to be transparent, sustainable and trustworthy to its constituents. For example, the well-known careerism that is endemic in academia, industry, governments and the 21st century workplace, or personal career interests of individuals, can taint the narrators' account of the innovation actors. Just as scientists are not immune to partisanship [10], innovation narrators are also rooted in the partisan fray, although latent it often may be. Yet narrators have so far not been subjected to this higher level of accountability, despite the trailblazing work of some 'bioethics observers' such as De Vries, Fox and Swazey, who have in essence advocated for an 'ethics of bioethics' or 'sociology of bioethics' so as to unpack and explicate these tensions embedded in an unchecked narrator role [11,12].

We propose the concept of a second-order narrator precisely to address this accountability gap among the classic first-order narrators, while recognizing and endorsing their importance in the postgenomics innovation knowledge ecosystem. Moreover, we suggest that for innovations to be integrated 'sociotechnically' and embedded in societal values and, therefore, be robust, as advocated by leading genomics R&D funding agencies such as the Wellcome Trust, Genome Canada and the NIH, we need such

nested and self-calibrating governance systems to respond to the uncertainties of biotechnology and postgenomic knowledge.

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The taxonomy of innovation as actors and nested narrator systems is also important for being truly inclusive in a manner informed by inherent power differences among the constituents of an innovation ecosystem. In effect, our proposed taxonomy guides decisions as to how we select different innovation actors in an engagement practice for innovations, and how we define inclusivity beyond the false face value of simply including some 'player' in a staging role. Much of the extant personalized medicine engagement exercises have been narrowly framed and do not include second-order narrators. In accordance with this, De Vries has aptly noted: "Sociology and bioethics have an uneasy relationship. Bioethicists find sociology helpful for describing and analyzing ethical issues, but they are less enthusiastic when bioethics becomes the subject of sociological scrutiny" [12].

This observation also underscores that the role of a second-order innovation narrator is not a popularity contest, and is subject to professional marginalization, but it is essential for credibility and long-term sustainability of personalized medicine innovations and building a 21st century knowledge society.

A taxonomy of actors and dual-order narrators takes the concept of innovation systems to a new level of stringency and standards. It is not a matter of simply thinking who is included or not, but instead thinking about the hitherto unchecked power systems and self-interests at play, and their consequential and collateral effects, on the postgenomics stage. These self-interests are neither necessarily malignant nor benevolent; interests and inescapable politics embedded in science and technology practice and, in due course, innovations, do exist [13]. Ultimately, the uptake of pharmacogenomics might be improved if both scientific and bioethics (and attendant social science, philosophy and law) institutions expressed an equivalent reflexive discourse; that is, being cognizant of how our own values and silent-value

commitments impact the conclusions we reach (e.g., ethical/unethical technology, person and company).

Taking innovations to the citizens of low- & middle-income countries

This interconnectedness matters, for there is another neglected but important aspect to consider for both sets of the innovation constituents: actors and narrators not only have self-interests, but may be reluctant to come out and engage or participate in the innovation ecosystems because doing so may risk their wellbeing, safety or careers. Consider, for example, the case of hypersensitivity reaction to abacavir, a nucleoside reverse transcriptase inhibitor drug used in persons with HIV infection. This serious hypersensitivity, occurring in up to 9% of persons receiving abacavir, has a strong genetic component associated with the MHC allele, *HLA-B*5701*. The genetic testing for this variant is now recommended in clinical guidelines and is practiced in most western countries [14]. However, advocating for availability or distribution of, or seeking, HIV therapy in many low- and middle-income countries (LMICs), let alone abacavir genetic testing for its personalized use, may trigger severe, irreversible social consequences. At the extreme but not uncommon end, it can lead to the disclosure of the HIV status of an individual. Stigma, ostracization and discrimination can result, with assumptions that an advocate is wrongfully aligned with an infected person who allegedly has a 'sinful' lifestyle, be it as a drug user, sex worker or lesbian, gay, bisexual and transgendered (LGBT) person, not recognizing (at the very least) that HIV is an epidemic that affects all of society.

Moreover, while citizens may turn to legal protection to combat these potentially negative reactions, there is a vast disconnect between 'the law on the streets' and 'the law in the books'; people who risk marginalization may find that turning to the law for support is limited or can even be futile in some LMICs [15]. Seen in this light, all the stage players cannot readily come together to build scientific knowledge. Narrators can serve the role of interactional expert advocates for marginalized innovation actors.

Moving outside our pharmacogenomics echo chamber for sustainable innovation

In the envisioned postgenomic worlds, upon which a stage of narrators and actors perform

innovative practices and deliver innovative technologies, we strongly advocate for the need to think outside our self- or socially assigned actor or narrator roles. Removing systemic obstacles to the health and wellbeing of all involves engagement in an innovation ecosystem that is truly inclusive both on paper and the streets, when technologies such as pharmacogenomics applications are being used for abacavir testing in LMIC for LGBTs and other marginalized groups.

"...advocacy on behalf of the disadvantaged groups is equally as important and should be carried out both by self-identifying members of these groups and also outsiders who believe in social justice as a principle."

Sadly, we still live in a world riddled with racism, sexism, xenophobia, anti-Semitism, bullying and homophobia. Moreover, 'extreme neutrality', that is, conscious indifference stemming from a self-serving desire to remain popular with those in power, is another endemic ill in our global society, be it in LMICs or non-LMICs. We in the field of public policy, science and technology studies, law, pharmacogenomics, public health and personalized medicine can do our part, starting with including LMIC LGBT individuals as a legitimate part of the discourse in technologies that affect them, as well as other marginalized groups such as women in LMICs who may benefit from certain genetic tests for drug therapy.

Engagement or advocacy on behalf of the disadvantaged groups is equally as important and should be carried out both by self-identifying members of these groups and also outsiders who believe in social justice as a principle [9,15,16].

In the current era, when pharmacogenomics application are often advancing to public health practice and from developed countries to LMICs, it is noteworthy that truly groundbreaking work is more likely to appear from marginal, dissident or unexpected sources, rather than from the well-established and entrenched powerful mainstream. While this is well recognized within the arts community (consider, for example, the innovative graffiti art and the chalk figures drawn by Keith Haring on New York City subway posters in the 1980s outside the exclusivist gallery and museum system [17]), the emergence of new unprecedented forms of public health pharmacogenomic knowledge will demand a keen knowledge of both global and local knowledge [18]. Only through such a

nuanced and integrated approach can a nested and freely engaged multilayer innovation ecosystem be designed and sustained, including in LMICs [9,19].

In the face of the deep fault lines that fracture 21st century human civilization and communities, which stand on an increasingly unsustainable and precarious pedestal, understanding the nature of innovation actors and first- and second-order narrators will pave the way not only for pharmacogenomics action on the streets, but also an open society [102] where the public can assume the role of actors as citizen scientists, as well as narrators of the first and second kind. Such hybridity is to be cherished, for it is intrinsically good and a *conditio sine qua non* for socially robust and sustainable postgenomic personalized medicine.

Authors' contribution

The idea of actors and dual-order narrators was proposed by V Özdemir in a former paper, wherein the concept of wiki-governance was proposed by ES Dove to operate such nested innovation knowledge ecosystems.

Disclaimer

The views and analysis reported herein are entirely the authors' personal opinions and do not represent the views of the affiliated institutions nor the funding agencies. Both ES Dove and V Özdemir are second-order narrators of post-genomics biotechnology and knowledge-based innovation. ES Dove is a sociolegal scholar and V Özdemir is a pharmacogenomics scientist and medical doctor by training.

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