Personalized Medicine Across Disciplines and without Borders. Vural Özdemir speaks to Hannah Wilson, Commissioning Editor

Vural Özdemir^{1,2,3,*}

¹School of Journalism, Faculty of Communications, Office of the President, International Technology and Innovation Policy, Gaziantep University, Gaziantep, Turkey

²Amrita School of Biotechnology, Amrita Vishwa Vidyapeetham (Amrita University), Amritapuri, Clappana P.O., Kollam, Kerala, India

³Data-Enabled Life Sciences Alliance (DELSA Global), Open Innovation Knowledge Platform, Seattle, Washington, USA

Abstract

Vural Özdemir began his career as a medical doctor in Turkey in 1990, as a scientist at the Faculty of Medicine, University of Toronto (ON, Canada), where he obtained his MSc and PhD in clinical pharmacology (1998), and subsequently completed a 4-year postdoctoral fellowship in personalized medicine with the late Werner Kalow, a founding pioneer in the field of pharmacogenetics. Özdemir contributed to the conception and development of the repeated drug administration (RDA) method as a novel way of measuring pharmacological heritability, pharmacogenetics of psychiatric drugs and studying the clinical role of *CYP2D6* genetic variations for endogenous neurotransmitter metabolism in the human brain. Recognizing that scientific knowledge is a product of both technology and social systems that often remain unaccounted for (e.g., human values, distribution of power and human agency, immigration, racial disparities, socioeconomic class and equity), Özdemir discovered the literature in the field of science and technology studies, a rich scholarly enquiry that asks fundamental questions and challenges assumptions regarding the backstage of technoscience, situates technology within its political context and makes hitherto unseen connections that frame science in ways that enable robust, responsible and sustainable innovation. From 2008 to 2012, Özdemir was awarded a mid-career “science and society” fellowship in order to retool as independent faculty and senior scientist in science and technology studies (STS), conducting research on research and examining his own trade – pharmacogenetics science – as an insider on the outside. Recently, Özdemir was awarded senior career support from the Scientific and Technological Research Council of Turkey, is an Associate Professor of both Communications and Human Genetics at the Faculty of Communications and serves as an advisor to the Rector for International Technology and Innovation Policy, Gaziantep University in Turkey. He is also a Visiting Professor (Global Health & Technology Foresight) at Amrita University in Kerala, India, and cofounder of the Data-Enabled Life Sciences Alliance (DELSA Global), an open innovation and knowledge translation platform in Seattle (WA, USA). Özdemir was named as coinventor of 12 World Intellectual Property Organization (WIPO) indexed patents in personalized medicine and has authored more than 130

*Correspondence: Vural Özdemir, MD, PhD, DABCP, vural.ozdemir@alumni.utoronto.ca.

peer reviewed articles and chapters on the translation of omics technologies into public health action, global technology governance, diagnostics innovation strategy, history of bioethics and the ethics-of-bioethics. ‘Science Peace Corps’ and ‘Microgrants for Big Data’ are two new knowledge translation and science communication concepts developed by Özdemir for the global governance of biotechnology. He is Editor-in-Chief of *OMICS: A Journal of Integrative Biology*, published by Mary Ann Liebert, Inc. (NY, USA).

Please could you give us a brief overview of your professional background to date?

I am a medical doctor and life scientist with a specialization in translational medical research to help move novel diagnostics into public health action on the ground, particularly in lower- and middle-income countries and in resource-limited settings in developed countries. In the last decade, I was trained in a second specialty as a scholar in political science, innovation and technology governance. Hence, I conduct, in parallel, *research-on-research* in order to examine the emerging novel scientific practices and the ways in which social and political systems shape technology innovation trajectories. These two strands of research in life science and political science, whose outputs are summarized in the biography in the abstract, have synergy and offer anticipatory insights into what lies ahead in the course of scientific innovation.

Put another way, technology provides answers (otherwise termed ‘solutions’) to natural science and medical dilemmas, whereas social science broadens those questions by making the backstage of scientific knowledge production transparent, accountable and thus more robust. An integrated technical and social science commitment builds the capacity to optimally respond to scientific uncertainties when innovation futures are still undecided and in the making.

What originally led you to work in the field of personalized medicine?

As a young medical student in the mid-1980s, I was curious about the large patient-to-patient differences in optimal doses required to treat each person. Such “variability questions” directly pertinent to personalized medicine were not on the radar back in the day, and were not included in most medical curricula around the world. My interest in personalized medicine was additionally cultivated by the influence of two mentors whom I was fortunate to have met in Toronto. The first mentor was the late Werner Kalow, who was a founder of the concept of pharmacogenetics and personalized medicine in Europe and North America, commencing in the 1960s. It was an instant intellectual connection since the first day we met in the early 1990s, beginning a long-term and productive discussion and testing of new ideas. As a postdoctoral fellow with Kalow, I began my dialog with a close collaborator of Kalow, Laszlo Endrenyi, who also became a mentor. Endrenyi was a sophisticated pharmacometrician and astute mathematician, in the European (Hungarian) tradition, who examined between-person and within person variations in pharmacological standard deviations and made biological sense of them in ways others could not.

Looking at a 2D scientific graph on paper and coming up with 3D deep biological insights was what Kalow and Endrenyi were often able to do effortlessly. To me, this was very inspiring intellectually as a young postdoctoral fellow.

Our collective work among the three of us, not to mention another scholar, Laszlo Tothfalusi in Budapest (a very fine pharmacometrician and deep thinker), paved the way for the invention and testing of the *Repeated Drug Administration (RDA) method* to measure the heritability of drug efficacy and safety. I discovered later that Endrenyi shared my interests in film and communication studies, particularly the French New Wave film directors' works in the 1960s that were in fact catalyzed by the use of a new "technology", *the hand-held camera*, which freed cinema from the confines of a rigid film set and took it out on to the streets. This began to formally broaden my interests in the social science aspects of personalized medicine and *point of care* "diagnostics on the go", as I have long believed that science in universities should connect with life on the streets and not be carried out merely for career advancement or self-interest; rather, it should be carried out with a sense of public duty and reflexive understanding of the broader societal impacts of our actions as a scientist. We must do science with the society in mind: a science by and for the people. I am grateful to both mentors, Kalow and Endrenyi, for cultivating in me the reflexive curiosity and courage to take the road less traveled and pursue "socio-technical" questions pertaining to drugs that some pharmacologists and scientists considered unimportant at the time. On that note, it is interesting to underscore that the discipline of social pharmacology, sadly, still does not exist to date in the 21st century.

While social medicine and social psychiatry do exist, for example, and drugs inextricably shape and are shaped by social and political forces, this blind spot in 21st century university design should be remedied before it is too late, as it directly impacts the equitable and broad uptake of pharmacogenetics and personalized medicine.

What do you think has been the most important development in the field of pharmacogenomics in the last 10 years?

I could cite many biomarkers and companion diagnostics that have been discovered and recommended to enable personalized medicine over the last decade. The availability of the next-generation sequencing technology and the reduction in the cost of many high throughput biomarker platforms are notable accomplishments. The adoption of multi-omics approaches (genomics, proteomics and metabolomics, and so on) are important, too, helping to keep the focus on the biological relevance and clinical utility of novel biomarker claims by triangulating data generated by complementary methodologies.

However, there is a more subtle and veritable progress being made. There is a slow but definite realization that technology alone will not deliver the much talked about disruptive innovations in personalized medicine. Certainly, the arrival of big data – which is actually a misnomer because it refers not only to large datasets but also to fast-moving data that are hard to validate – calls for *social innovation* to work with the end-user communities in order to bring about truly novel innovations. Such user communities (patients, developing world citizens and hitherto marginalized communities, among others) often know what works best

‘in the field’, well outside the academic ivory tower in terms of addressing unmet needs. These end users, too, could and should participate in scientific design and offer innovative ways to translate big data into concrete health outcomes.

Put in other words, we need a greater emphasis – and this is happening – on *independent* social and political science analyses of personalized medicine technology in order to cultivate the disruptive innovation capacity with a much larger set of stakeholders that extends beyond the classic academia, industry and government triad.

You have done a lot of work on personalized medicine in resource-limited settings. What is the status of this and what are the next steps?

Advances in communication technologies and perhaps, as a positive outcome of globalization, the old binary of “developed versus developing world” is no longer valid. Scholarship does not recognize geography, and innovation can emerge from pretty much anywhere in the world.

I like to look at science and the world without preconceived notions as much as humanly possible. In addition, to make sense of Big Data-driven personalized medicine, we cannot exclude any world community, developed or developing, for lack of a better phrase.

This is required not only on principled ethical grounds, but also in order to cultivate disruptive innovations by user communities, as I have noted above. The current situation in resource-limited settings is a “glocal” (global plus local) challenge and opportunity. This is in fact a common challenge in developed countries as well. We are facing and occasionally witnessing the clash or incompatibility of global norms with local norms (and *vice versa*); this tension is more pronounced in resource-limited settings.

In the face of such glocal tensions, there is a need for dialog between the local and global interests and norms and to prevent the exploitation of local communities, but also to recognize the global nature of science and certain universal (transnational) norms, such as human rights. The minimum threshold that needs to be maintained in order to resolve glocal conflicts in the course of personalized medicine science is to respect basic human rights and not allow them to be breached.

I should underscore that the fascination with new technologies appears to be widespread (and arguably hyped) in resource limited settings, with relatively less emphasis on their real-life utility. This is certainly the case, for example, with pharmacogenetics tests. In the absence of a sound capacity for independent critical examination of the claims made for personalized medicine diagnostics, many in resource-limited settings could suffer from (un)trustworthy expertise claimed by pseudo-scientific actors.

Still, I remain optimistic that resource-limited settings are really interesting and timely places to make a concrete and ethical contribution to personalized medicine, especially by virtue of the fact that these large populations are in need of rational therapeutics.

We should not forget, however, that personalized medicine can also be accomplished with already-available tools (e.g., by harnessing existing guidelines in order to prevent drug–drug interactions). We need to address the “know/do” gaps where existing knowledge is not utilized in resource-limited settings. Setting up a drug–drug interaction information office in a hospital or city center can go a long way in resource-limited settings, in much the same way that setting up advanced technology-driven biomarker laboratories would. Sometimes there are simple solutions to complex problems!

What is the role of migration as a factor for consideration in personalized medicine?

Much of the lore in the personalized medicine field has rested on an unchecked assumption that human populations are static, “settled” or entrenched in a given geographical locale. Migration, I should note, is not only physical but also virtual. With social media and communication technology, one can migrate far and fast physically and/or virtually. This can impact the entire research and development trajectory, including subject recruitment, the delivery of personalized healthcare and the turnaround times necessary to return test results in a migrant population that may not be there in a few days time. We are currently working on global personalized medicine in southeast Turkey with the arrival of refugees across the Syrian border, some of whom are medical doctors. This puts a new and human face on the map, whereby one has to recognize that one can be both a refugee and a doctor. Such dual or hybrid identities demand a social science lens in order to design and implement personalized medicine in a way that makes sense to a globally diverse world population with multiple identities, owing in part to physical and virtual migration.

Can we overlook a societal factor that impacts human lives so dramatically with regards to the design and implementation of personalized medicine? Both are part of life and warrant due consideration.

What do you think should be the role for scientists in engaging in social and political research in personalized medicine?

This is an important and yet difficult question to answer in limited time. Let us say that genomics and other life sciences answer important questions about natural systems and human pathophysiology, whereas social science, and political science in particular, teach us which questions to ask, whether there are biases in the questions being asked in the first place and, overall, to make sure that we do not find the “*right answers to the wrong questions*”.

For example, in a refugee population in flux with a high prevalence of infectious diseases, research might need to focus, at least initially, on that very question rather than other long-term end points, such as cancer susceptibility. Moreover, in the case of big data, where no single consortium has the scale to translate it into innovative products, political science helps to understand the ways in which science can engage with society for collective innovation,

thus leaving behind the old notion of science as a romantic insular activity taking place solely in a laboratory.

What are the barriers to this?

Natural science and social/political science are long lost siblings who need to be reunited. As a result of the modern university system, they have been artificially separated over the past few centuries. In order to appreciate their equal relevance, it suffices to remember that the moment one steps into a laboratory, the illusion that science is a value-neutral and apolitical act dissolves rapidly. Yet most if not all scientists in the past 400 years have tended to believe in the romantic but self-defeating idea of science being apolitical, and they are surprised when they encounter politics on a day-to-day basis (what we can call “micropolitics”).

With politics, I refer to the entire constellation of situations in which “*what is apparent or expressed*” differs distinctly from “*what is actually intended or at work*”.

Even a simple smile can be political if it is meant to influence others for a particular interest and outcome or to maintain a system of control. In order to overcome this epistemological barrier among scientists, the alternative is to engage in politics intelligently (i.e., not sweep it under the carpet and think it will go away) through political science research, for example, so as to make the embedded politics and thus science and innovation more transparent, robust and responsible.

If we truly believe in science, then such commitment to social and political science is a precondition for a socially attuned personalized medicine science, which can then remain broadly respected, independent and responsibly innovative. Ultimately, the real risk is not in politics, but in being ignorant of politics; by not permitting its ‘unpacking’, robust scientific inquiry is threatened.

I shall note in this specific context that no one is above the fray when it comes to the political. Such reflexive thinking is relevant not only for life scientists, but also for social scientists and bioethicists who are not necessarily immune to these same political influences. Professional designations such as life scientist, social scientist, bioethicist do *not* automatically render individuals ethical or reflexive, and no person is “above the fray” in the latter context. The fields of sociology of bioethics and the ethics-of-bioethics reflexively examine these very important and yet overlooked *second-order questions* in personalized medicine. I refer the reader to our short analysis published this year in the journal *EMBO Reports* entitled “The epiknowledge of socially responsible innovation”.

What do you plan to work on next?

“Science Peace Corps” and “Microgrants for Big Data” are two new concepts we have developed for global governance of technology and innovation in the field of personalized medicine. We are working to implement these steering tools and measure their socio-technical impacts on science and society. These new biotechnology governance instruments offer ways to create new political fora for disruptive innovation and “extended peer-review”

of science, technology and knowledge-based innovation, particularly in resource-limited settings, hitherto marginalized groups (e.g., rural communities) and end-users of innovations.

What is the role for global collaborations, such as the Genomic Medicine Alliance, in the issues we have discussed? Where do you envisage the field as a whole progressing in the next 5–10 years?

The bottleneck in genomic medicine has shifted markedly from data generation to analysis and deriving value from data and, importantly, demonstrating the clinical and public health utility of biomarkers. This effort requires that upstream science (i.e., the design of experiments) and downstream implementation in user communities come together. This is both a technical and sociological challenge. For this translational science to materialize, both resource-rich and resource-limited regions need to work together. The Genomic Medicine Alliance is one of the globally leading collaborations that makes contributions in all of the above important contexts.

The concept of an “alliance” is innovative, much more feasible and certainly powerful than classic consortia science, as it has *the best of both worlds*: the scale of large collective science and yet the flexibility and adaptability of small artisan science groups. I support the concept of an alliance wholeheartedly, more so than traditional consortia that are not always scalable, inclusive or flexible in a global, ever-changing world in flux.

Alliances such as the Genomic Medicine Alliance are well poised to deliver on the realistic promises of genomics in the next 5–10 years and perhaps much sooner, in the “developed and developing world” alike, and doing so in the spirit of responsible innovation, whereby ethics research is well informed by the social sciences.

Finally, I feel compelled to emphasize that collective innovation, as a term, should remain truthful and loyal to its ethos: the cultivation of responsible governance for *all* constituents, and not only for a selected few.

Is there anything else you would like to add?

For every story told, there is an untold story about science and innovation. Working across the disciplines, natural sciences, social science and humanities, and without borders around the world with due respect for local cultures and human rights is not an easy or simple endeavor. Nor is it invariably popular, as it changes the old ways of doing things, reshapes the entrenched sociotechnical power networks, but it is essential for the credibility and long-term sustainability of personalized medicine innovations and building a 21st century knowledge society.

Taking the roads less traveled, which are often outside the mainstream disciplinary dogmas, is something I would like to advise to young scholars and students in their future science careers. It may not bring them immediate tangible rewards such as financial success, but the intellectual and societal rewards are many, enduring and priceless.

Times are changing indeed for global personalized medicine science. In the end, I believe in the idea of living and working not only for the current status quo but also imagine multiple possible future(s) that are more sustainable, reflexively ethical and equitable and thus, work towards them. I was fortunate to have many friends around the world who encouraged me steadfastly to continue on an interdisciplinary and integrative path for personalized medicine. I wish to thank them, as well as the editors of *Personalized Medicine*, for the opportunity to present my candid views as they truly are. I feel an obligation to share these views, especially for the young scholars and students interested in personalized medicine and disruptive responsible innovation, so that they are best informed on the paths and exciting career futures that are available to them.

Acknowledgments

The analysis, concepts and work reported herein were informed and supported by the following research grants to Dr. Özdemir: Canadian Institutes of Health Research (CIHR) operating research grant, number 84620, on pharmacogenomics and society research, and grants from the Social Sciences and Humanities Research Council of Canada and Genome Canada on emerging biotechnology foresight research. Helpful peer comments and feedback by editors are gratefully acknowledged.