

EDITORIAL

A Transdisciplinary Forum for Study of Individual and Population Variability in Response to Health Interventions and Personalized Medicine

We are pleased to introduce the September issue of *Current Pharmacogenomics and Personalized Medicine (CPPM)* and share with you the editorial vision of the Journal as an integrated new title addressing both pharmacogenomics and personalized medicine readership effective 2008. *CPPM* has a unique focus on the complex challenges and promises emerging from the fusion of knowledge domains in therapeutics and diagnostics (i.e., theragnostics) in postgenomics medicine. The Journal covers issues relating to individual and population variability in drug treatment outcomes and disease susceptibility. A firm understanding of these variability questions is a prerequisite and essential foundation to achieve the overarching goal of personalized therapeutics [1-4]. We bear in mind the increasingly globalized nature of health research and services, and the diverse technologies, stakeholders and interdisciplinary expertise that collectively drive the rapidly evolving knowledge frontiers in personalized medicine.

The September issue in front of you features articles that offer a transdisciplinary synthesis of the recent developments in the field. Tikki Pang asks the question if it is "too soon", or "just-in-time" for the developing countries to consider the applications of pharmacogenomics in dealing with priority health problems. In the face of genomics research that now extends well beyond the laboratory bench to global society [5, 6], and pandemics that do not recognize national and geographical borders [7], this article makes a timely contribution at the unique intersection of personalized medicine and global public health. Following on the latter theme, Muin Khoury provides an in-depth account of the public health genomics, a multidisciplinary field concerned with the effective and responsible applications of genome-based knowledge and technologies to improve population health.

Blood-based biomarkers of devastating mental illnesses have been pursued for many decades with only equivocal success. Stephen Glatt and colleagues now provide an exciting new perspective on the promise of blood-based biomarkers of major psychosis by measuring the transcriptome and querying the "exome" (all exons) and "spliceome" (all alternatively spliced variants). While exploratory in scope, this original research has considerable conceptual implications to measure and monitor time-dependent changes in disease severity and response to therapeutic interventions in psychiatry. At this critical juncture in postgenomics medicine when genes are increasingly viewed as fluid hereditary units highly responsive to the environment (instead of the previous views of genes as rigid and static entities), appreciation of the dynamic plasticity of the human genome is crucial and timely.

As personalized medicine research is moving full steam ahead, there are important transdisciplinary lessons to be learned from individualization of health interventions other than drugs [8-12]. With this in mind, the June and September issues of the *CPPM* provide a special focus on the nascent field of nutritional genomics and personalized dietary interventions. Douglas Ruden and colleagues present herein a critical synthesis of the work in the field of evolutionary biology in *Drosophila* models as a complement to human nutrigenomics. They also aptly indicate the anticipated increase in statistical power in using inbred *Drosophila* lines that are freely available to investigators. In reference to the ethical challenges raised by nutritional genomics, Béatrice Godard and Thierry Hurlimann note that different forces may drive the choice of research priorities and shape the claims that are made in this new convergence of genomics and nutrition science. The *CPPM* will continue to monitor these and similar complementary advances in personalization of health interventions and facilitate knowledge transfer and synthesis across the disciplinary boundaries.

In study of drug metabolism and medical specialties such as psychiatry and oncology, pharmacogenomics and personalized medicine have been intensively pursued over the past several decades [13-15]. By contrast, ophthalmology and certain other therapeutic areas relatively lagged behind. Diabetic retinopathy is a significant public health burden and remains as one of the leading causes of blindness. Current treatments are only marginally effective with marked person-to-person variation in treatment outcomes. Gregory Liou and colleagues present a synthesis of their preclinical findings on cannabidiol, a non-psychoactive native cannabinoid, as a potential treatment for diabetic retinopathy. They underscore that understanding the biological action of cannabidiol in preclinical models can offer a conceptual map and a rational departure point for development of biomarkers of cannabidiol action in clinical studies. Although such novel preclinical observations need to stand the test of future clinical investigations, they warrant consideration in a context of targeted therapy to individualize new treatments and address the unmet needs of the patients with diabetic retinopathy. Finally, Tomlinson and colleagues announce the International Conference on Personalized Medicine in Hong Kong and its significance for regional and global integration of research activity in personalized medicine. The articles in the September issue thus collectively illustrate the new transdisciplinary forum created by the *CPPM* and our integrative editorial focus on personalized medicine and the enabling technologies. We aim to bring expert views from authors in diverse global regions internationally after rigorous and independent peer review. Importantly, in order to maximize the transparency, quality and completeness of reporting of genetic association findings, the *CPPM* is one of the first biomedical journals to proactively encourage the authors to consider the recent STREGA recommendations as articulated in the Journal author instructions [16]. In parallel, as we write these lines, we are witnessing the timely intersection of epidemiology and pharmacogenomics in the form of "pharmacogenomic epidemiology"; the latter new hybrid field assesses

the range of responses to pharmacologic agents in relation to genetic variation in population groups [17]. These developments collectively attest to the importance of multidimensional debates on personalized medicine and pharmacogenomics [18].

CONCLUDING REMARKS

In therapeutic drug monitoring, there is an age-old maxim that cautions to “treat the patient, not the laboratory test”. To this end, it is noteworthy that pharmacogenomics is an important biotechnology application to understand the genomic basis of variable drug effects but it needs to be cross-validated and complemented by other approaches such as phenotypic measures of drug metabolism, pharmacoproteomics, nanotechnology-based customized drug delivery, systems biology, evidence based personalized medicine policies that aim to strengthen global health systems and services delivery, and so on. What is appropriate, then, is not to rely on a singular technology but instead consider whether and to what extent a battery of biomarker tests or new health technologies explain variability in response to medicines in a mechanistic and clinically relevant manner, within the context of global health systems.

Personalized medicine applications, and innovations more generally, are not autonomous value-neutral activities but are embedded in a social and political context [6]. Even though personalized medicines may, on the one hand, threaten the classical economic models and pharmaceutical markets that historically depended on the “one-size-fits-all” blockbuster model of drug development, we anticipate that the demand for personalized medicines will exponentially increase in the near future as we move towards an era of comparative effectiveness [19], and be further shaped by consumer responses, the needs of global population health and considerations for international human rights [20, 21]. A peer-reviewed international forum that provides credible and in-depth evaluation of personalized medicines and related biotechnology applications is therefore timely and essential [18, 22, 23].

In a discussion of the innovation systems more than a decade ago, David and Foray concluded that “an efficient system of distribution and access to knowledge is a *sine qua non* [cannot do without] condition for increasing the amount of innovative opportunities” [24]. We wish to add to this historical context that the future cultivators of personalized medicine innovations will not only have to keep an open, vigilant and discerning mind but also need to acquire qualities and training to be “semantic translators” of new knowledge across diverse disciplines, beyond merely presenting a composite summary of data [25]. Hence, as *CPPM* Editors, we will continue to give voice to new ideas, including those from junior investigators, and inclusively from different corners of the world. We will also peer review articles that provide empirical data from social science analyses of personalized medicines or a reasoned and balanced discussion of the social, ethical, economic, legal and policy aspects.

Editors need to maintain a “sixth sense” to keep abreast of new developments and innovations before they actually crystallize in the field. While we strive to achieve a forward looking, anticipatory and synthetic editorial vision, we welcome your expert reviews and original research that offer unique insights and concretely address the present and future unmet needs in the field.

REFERENCES

- [1] Sheiner LB. Learning versus confirming in clinical drug development. *Clin Pharmacol Ther* 1997; 61(3): 275-91.
- [2] Reidenberg MM. Evolving ways that drug therapy is individualized. *Clin Pharmacol Ther* 2003; 74: 197-202.
- [3] Kalow W, Ozdemir V, Tang BK, *et al*. The science of pharmacological variability: an essay. *Clin Pharmacol Ther* 1999; 66(5): 445-7.
- [4] Cohen N. *Pharmacogenomics and Personalized Medicine*. Totowa, NJ: Humana Press 2008.
- [5] McNally R, Glasner P. Survival of the gene? 21st century visions from genomics, proteomics and the new biology. In: Glasner P, Atkinson P, Greenslade H, Eds. *New Genetics, New Social Formations*. London: Routledge 2007; pp. 253-78.
- [6] Ozdemir V, Suarez-Kurtz G, Stenne R, *et al*. Risk assessment and communication tools for genotype associations with multifactorial phenotypes: the concept of “edge effect” and cultivating an ethical bridge between omics innovations and society. *OMICS: A Journal of Integrative Biology* 2009; 13(1): 43-61.
- [7] Poland GA. Pharmacology, vaccinomics, and the second golden age of vaccinology. *Clin Pharmacol Ther* 2007; 82(6): 623-6.
- [8] Darnton-Hill I, Margetts B, Deckelbaum R. Public health nutrition and genetics: implications for nutrition policy and promotion. *Proc Nutr Soc* 2004; 63(1): 173-85.
- [9] Kapat J, Perlina A, Hatipoglu B, *et al*. Nutrigenomics: concepts and applications to pharmacogenomics and clinical medicine. *Pharmacogenomics* 2007; 8(4): 369-90.
- [10] Caudill MA, Dellschaft N, Solis C, *et al*. Choline intake, plasma riboflavin, and the phosphatidylethanolamine N-methyltransferase G5465A genotype predict plasma homocysteine in folate-deplete Mexican-American men with the methylenetetrahydrofolate reductase 677TT genotype. *J Nutr* 2009; 139(4): 727-33.
- [11] Robitaille J. Nutrigenomics and personalized diet: what are the anticipated Impacts for research on chronic diseases and public health? *Curr Pharmacogenomics Person Med* 2009; 7(2): 106-14.
- [12] Ferguson LR. Epigenetic variation and customizing nutritional intervention. *Curr Pharmacogenomics Person Med* 2009; 7(2): 115-24.
- [13] Eichelbaum M, Spannbrucker N, Dengler HJ. N-oxidation of sparteine in man and its interindividual differences. *Arch Pharmacol* 1975; 287: R94.
- [14] Mahgoub A, Idle JR, Dring LG, *et al*. Polymorphic hydroxylation of debrisoquine in man. *Lancet* 1977; 2: 584-6.
- [15] Nebert DW, Zhang G, Vesell ES. From human genetics and genomics to pharmacogenetics and pharmacogenomics: past lessons, future directions. *Drug Metab Rev* 2008; 40: 187-224.
- [16] Little J, Higgins JP, Ioannidis JP, *et al*. Strengthening the REporting of Genetic Association Studies (STREGA): an extension of the STROBE statement. *PLoS Med* 2009; 6(2): e22.
- [17] Guessous I, Gwinn M, Yu W, *et al*. Trends in pharmacogenomic epidemiology: 2001-2007. *Public Health Genomics* 2009; 12(3): 142-8.
- [18] Llerena A, Michel G, Jeannesson E, *et al*. Third Santorini conference pharmacogenomics workshop report: Pharmacogenomics at the crossroads: what else than good science will be needed for the field to become part of Personalized Medicine? *Clin Chem Lab Med* 2007; 45(7): 843-50.

- [19] Woodcock J. Chutes and ladders on the critical path: Comparative effectiveness, product value, and the use of biomarkers in drug development. *Clin Pharmacol Ther* 2009; 86: 12-4.
- [20] Quick JD. Ensuring access to essential medicines in the developing countries: a framework for action. *Clin Pharmacol Ther* 2003; 73: 279-83.
- [21] Hogerzeil HV. Essential medicines and human rights: what can they learn from each other? *Bull World Health Organ* 2006; 84(5): 371-5.
- [22] Javitt G, Katsanis S, Scott J, *et al.* Developing the blueprint for a genetic testing registry. *Public Health Genomics* 2009 Jun 29 [Epub ahead of print].
- [23] Ozdemir V. Science policy and knowledge translation in the post-genomics era: A proposal for an 'Essential Diagnostics Library'. In: Symposium: Bridging the Continents in Istanbul: Personalized & Predictive Medicine in Turkey - Too Soon or Just-in-Time? Yeditepe University, Istanbul, September 2009 (in press).
- [24] David P, Foray D. Assessing and expanding the science and technology knowledge base. *STI Review* 1995; 16: 13-68.
- [25] Gardner H. *Five Minds for the Future*. Boston, MA: McGraw-Hill Ryerson Agency 2007.

V. Ozdemir

Department of Social and Preventive Medicine
Department of Psychiatry, Niigata University
Faculty of Medicine, University of
Montréal, Montréal, Québec, Canada
E-mail: vural.ozdemir@umontreal.ca

T. Someya

Graduate School of Medical and
Dental Sciences, Niigata
Japan
E-mail: psy@med.niigata-u.ac.jp