



Editorial for the inaugural issue

The new Journal of Applied & Translational Genomics: No, not just another new journal



Knowledge without justice ought to be called cunning rather than wisdom. Plato

Welcome to the newly revamped journal of Applied & Translational Genomics (ATG). ATG is a new open access biomedical journal providing a global forum for 'omics' research, converging disruptive technologies, clinical genomics, and related issues in education, bioethics, public health, citizen science and policy. The journal's mission is to enhance knowledge sharing and discussion of applied and translational genomics worldwide. With the assistance of my committed and esteemed Editorial Board members, ATG will reach deep into otherwise less recognized and resourced areas of the world to give voice to quality research, analyses and commentary. Thus, the new ATG is a bold, but nonetheless important, initiative.

This inaugural issue covers key cutting edge interdisciplinary areas at the forefront of translational and applied genomics and thus differentiates the journal. In content, we cover original research, an analysis of the meaning of translational genomics, a report on convergent innovative informatics applications and another on proposed initiatives to improve the integration of a molecular approach to targeted cancer medicine, database and data infrastructure reviews, a commentary, a FDA regulation and consumer rights to access their genome and a correspondence.

Of paramount importance is Kussman and Kaput's 'Translational Genomics' because it lays out the journal's definition of the 'translational and applied genomics', clarifying what we mean, and what we do not mean. Historically, 'applied' research was considered a development (R & D) and as such distinct from basic, pre-clinical, research. The view of the authors, and the journal for that matter, is that a new meaning is more apt. Translational and applied genomics now incorporates the relatively nascent fields of systems thinking, real time monitoring, big data, and predictive analytics, evidence-based solutions and patient participation at all points in the lifecycle. In this way, translational research focuses on 'relevance' to human health. The authors articulate how and why translational human genomics research extends functional science to include the use of 'omics' to capture the dynamism of biological processes and environmental exposures. With this new focus, translational omics will increasingly make use of longitudinal data generated by the ever more quantified individual, combining 'the best science with applications in real time', thus debunking the idea that 'translational' and 'basic' research are distinctly different activities. In sum, Kussman and Kaput convincingly show how this new definition of translational omics research can generate high impact solutions applied in real time to assess, mitigate, improve or delay disease symptoms, and thus maintain health.

Artificial super intelligence is rapidly expanding its grip on basic tasks of everyday life. The increased use of sequencing and real time monitoring data output far outpaces our ability to harness and effectively use it. Engineered intelligent software systems are emerging to meet this need. Naik and Bhide provide a brief update and reflection of how these intelligence systems automate routine cognitive tasks used in knowledge processing and thus solve significant gap in utilizing and understanding generated data in a unified platform.

The authors explain how second generation automated knowledge management is accomplishing complex and varied workflow tasks in genomic research. High throughput screening (HTS), next generation sequencing, genome, exome and ome sequencing are clearly generating massive amounts of biological data. HTS quickly conducts a large number of pharmacological, chemical or genetic tests. NGS sequences RNA transcriptomes to produce high definition views of transcript sequence, SNP haplotypes, rare variants, splicing, exon boundaries and RNA editing. Automated technologies can swiftly sift through existing knowledge to identify, tag genes, antibodies or active compounds in real time. Accomplishing such complex and varied tasks requires computer intelligence that can learn, namely, continually build on the new knowledge it generates, not just do. Naik and Bhide artfully describe two different Opra solutions for genomic knowledge management; Opra Bio-NLP that generates genomic knowledge from the biomedical literature and then auto-populates it into legacy databases; and a platform that detects, demarcates and annotates regions of interest in medical imaging. Challenges to ensuring that these systems are full-proof and concomitant ethical issues are raised.

It is widely known that tumor heterogeneity is common within and between tumors, and affects both cancer pathways and phenotypic variation. Tumor sample heterogeneity is a limitation in somatic mutation detection and thus challenge to personalized cancer medicine. Watanabe et al. report their success in overcoming detection limitations due to heterogeneity. Using simultaneous genome and single cell identification using semiconductor based next generation sequencing they were able to discriminate A549 cancer cells from a bulk population of A549 cells, thus eliminating the problem of somatic variant detection in the presence of tumor heterogeneity. The success of their approach is an important step forward in both overcoming the limitations of current somatic mutation detection methods and personalizing oncology.

Knowledge derived along the path from variant detection to variant interpretation to clinical significance is frequently discussed but a detailed analysis of the basis for limitations in that 'knowledge' is infrequent at best. Quintans et al. contribute a thorough elucidation of these limitations and difficulties. Imprecise and incorrect use of terms results in mischaracterizations and falsely attributed causation. Further,

risk of misinterpretation derives from biased content, such as biorepository interpretation is based only on annotations of variant functional consequences using databases stored in, or linked to, the same repository. The authors further show how stepwise and linear interpretation processes are likely to overrate some pieces of evidence while underrating others. They call for accurate and consistent use of terms and algorithms that permit a multidimensional parallel analysis of diverse evidence for specific genes, cellular pathways or disorders. Their conclusion reinforces the appropriateness of Kussman and Kaput's definition of translational genomics.

Bennetts et al. report the new collaborative effort on the part of the Human Variome Project (<http://www.humanvariomeproject.org/>), the Royal College of Pathologists of Australasia and the Human Genetics Society of Australasia to develop quality standards for gene variant databases. The authors briefly discuss some of the many initiatives, white papers, best practices, policy statements and guidelines that address aspects of responsible integration of emerging genomic technologies into mainstream clinical diagnostics. The collaboration is designed to establish standards for accuracy, quality and ongoing data maintenance to ensure that a data repository meets the needs of the clinical diagnostic environment. When completed, the project will have demonstrated the feasibility of creating a networked quality data standard that is aligned with both existing laboratory standards and accreditation requirements, as well as guidelines and new initiatives while setting minimum requirements for clinical purposes within the boundaries of existing national and global legislation. This achievement will mark an important step in advancing the clinical application of gene variant knowledge.

The path from available molecular based technologies and treatments to individual and societal benefits of targeted cancer medicine is lined with challenges in aligning proven clinical research with care delivery systems. Leading research and clinical oncology experts recently convened to identify top unmet needs and recommend solution strategies. Flynn and Van Dam report on eight strategic initiatives ranging in scope from the need for a sustainable patient/tumor genotype/phenotype registry for research and clinical use to better dissemination of new clinical knowledge and tools to community care providers who lack the resources of large academic medical centers.

Without people there is no translational and applied genomics. For this reason, some bioethicists argue that justice commands reciprocity between researchers and donors, in part because in practice reciprocal rights and obligations are not the norm. Regulation of access to genomic information intends to fairly balance society's right to protect the public against the effects of ineffective and harmful genomic technologies, and a person's right to learn what's in their genes. However, the balance of burdens and benefits set is not without controversy on various levels. Angrist analyzes the 23 & Me/FDA debacle as a case in point, raising important questions about when and how regulation can inappropriately stand in the way of people, healthy or sick, and their genomes.

Note that we publish a letter to the Editor regarding the use of Hardy-Weinberg equilibrium in the previous ATG article "Association of polymorphism in cytochrome P450 2C9 with susceptibility to head and neck cancer and treatment outcome" (Yadav et al., 2014). We encourage correspondence and lively, even provocative, discussion.

Finally, in the Apology, Plato writes, "the greatest good for a man (is) to discuss virtue (excellence) every day and those other things about which you hear me conversing and testing myself and others, for the unexamined life is not worth living for men." (38a) A life focused on the question of its greatest good is a life lived to its fullest, that is, an excellent, or virtuous, life. Plato's concept of wisdom emphasizes the need to put understanding into practice; to make a difference not only in one's life but also in the lives of others. The journal's view is that translational and applied genomics instantiates knowledge into practice and in doing so makes a difference in the lives of all, wherever situated around the globe.

Reference

- Yadav, et al., 2014. Association of polymorphism in cytochrome P450 2C9 with susceptibility to head and neck cancer and treatment outcome. *J. Appl. Transl. Genomics* 3 (1), 8-13.

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