



## Editorial

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This issue contains several regular articles along with a featured special section on lifestyle genetics. Written by researchers and experts from around the world, the breadth of topics covered reflects both multidisciplinary and global contributions to advancing applied and translational genomics, as defined in previous issues.

The regular articles cover original research, a case report, and topical issues in big data, reimbursement, and education. The research article and case report contribute to the scientific need for genomics to be more globally diverse, particularly in low resourced nations. In 'NGS Meta Data Analysis for Identification of SNPs and INDELs Pattern in Human Airway Transcriptome: A Preliminary Indicator for Lung Cancer', Dr. Sathya et al. report preliminary results of SNPs and INDEL discovery in the human airway transcriptome of individuals with and without lung cancer and who are or aren't smokers in efforts to identify SNP and INDEL patterns responsible for lung cancer in India. Lung cancer incidence is on the rise in India. Recent research estimates that 87% of males and 85% of females with lung cancer have a history of active tobacco smoking. Passive tobacco exposure has been linked to 3% of all cases and a recent meta-analysis of 41 studies showed that the risk of developing lung cancer increases with increased exposure.<sup>1</sup> Using next generation sequencing, the authors found 5 SNPs and 2 INDELs in the SCGB1A1, SCGB3A1 and NKFB1A genes of smokers, suggesting a signature for disease pathogenesis. Findings are preliminary, requiring more analysis and wet lab validation, yet they provide a resource for further genetic studies of smokers and the development of precision medicine.

Dr. Ben Brahim reports a unique case of Beckwith–Wiedemann Syndrome (BWS) in Tunisia. She reports on a novel form BWS, in 'Partial KCNQ1OT1 Hypomethylation: a Disguised Familial Beckwith Wiedemann Syndrome as a Sporadic Adrenocortical Tumor'. Molecular analysis of an infant presenting with an adrenocortical tumor, and a family history of such tumors, revealed partial KCNQ1OT1 hypomethylation and complete loss of methylation in the adrenocortical tumor. Incomplete penetrance and specific tissue mosaicism are thought to explain the new presentation.

This issue's news & views report proceedings of an expert panel discussion on big data challenges and key strategic needs in precision medicine, held at the 6th annual Personalized Medicine Partnership meeting, Arrowhead Publishers, 2014. Translational bioinformaticians representing a broad range of expertise delivered an informative and lively presentation. Experts defined the problem, identified specific unmet needs and emerging trends in knowledge generation methods and analyzed consent restrictions. While important shifts to cloud storage, open collaborative platforms and integrated approaches

have occurred, they agreed that data complexity is precision medicine's challenge to solve.

Dr. Hafez's commentary 'Precision Medicine is Here, Break Out Your Wallet' challenges the notion that precision medicine is really here, based on the economic realities of the U.S.'s health care system. When technological feats such as the \$1000 genome are pitted against earning reports of large publically traded companies offering genetic testing and significant financial losses and reduced Medicare reimbursements, Hafez argues, it is readily evident that payer and clinical adoption of genetic testing is lagging behind technological capabilities. He explains why major reimbursement policy is needed if precision medicine is to attain its promised goals.

Clinical adoption of genomic advances is constrained not only by reimbursement issues but also by family physicians' lack of sufficient knowledge and skill, particularly in regard to handling emerging ethical issues. Zawati et al. present a pilot study designed to address these unmet educational needs through a comprehensive multi-pronged training strategy. 'Ethics Education for Clinician-Researchers in Genetics: The Combined Approach' discusses the development, implementation and learning satisfaction of the conference delivering the novel approach. They recommend adoption by medical schools, clinics and hospitals and results of such programs will be instructive.

### Lifestyle genomics

Advances in epigenetics and understandings of the dynamic relationship between genotype and phenotype have led to increasing research interest in overlaps between lifestyle and genomics. An upshot is that once disparate domains of research, lifestyle and genomics, are now working together to unravel mysteries.

The purpose of this special section is to present this initiative and current research in various countries.

The article by Lucivero and Prainsack, discusses how direct-to-consumer testing is typically used. Although laws in the different countries vary in limitations imposed on companies selling DTC kits, a person can often buy kits and take a test, e.g. swab the inside of their cheek or spit saliva into a cup, in the privacy of their home and soon thereafter learn if they are likely to be affected by cancer, or some other affliction, in the coming years. Regulators and ethicists have questioned whether DTC tests are appropriate since they hit the market more than a decade ago. The authors analyze frequently raised issues such as concern about the use of a test not clinically validated, or the reporting of a wrong result. What is the ethical impact of all this? Should governments protect users from harm? Should individuals have the right to take such tests in the name of genetic tourism or genetic recreation?

Nutrigenomics, often referred to as nutritional genomics, is the investigation of the relationship of diet and genes to health and disease.

<sup>1</sup> Behera, D., Lung Cancer in India. *Medicine Update* 2012 vol. 22, 401–7.

Nutrigenetics, often used interchangeably with nutrigenomics, is a sub-discipline that examines the association of gene variants (SNPs) with intermediate risk factors, such as glucose response.<sup>2</sup> Commercial nutrigenomic tests have promised people a scientific way to choose a diet that optimizes their health. However, the science supporting the test and its result is often lacking, as Pavlidis et al. discuss. They explain the scientific complexities and why commercial promises of optimal health through a scientifically proven optimal diet are illusory. Further, they discuss the fact that despite scientific advances in nutrigenomics, there is not a definite scientifically supported way of applying research findings. In analyzing the clinical and commercial impact of the field, they point to research 'gaps' and identify what current literature says and importantly doesn't say.

How an individual's genes influence their athletic ability, the genomics of exercise, is another budding field in lifestyle genetics. Among questions currently researched is how do systems as renin-angiotensin influence the way that the genes and certain genotypes respond to them? The article by Van Ginkel et al. investigates the way that the renin-angiotensin system could be influenced during exercise in the ACE I/D gene polymorphism, suggesting that genes play important roles in regulatory systems.

Arguably, one of the overarching goals of lifestyle genetics is to determine how to maximize health for the longest period of time. Research on the genetics of longevity has been underway at several institutions for at least a decade. Govindaraju et al. provide a thorough analysis of how longevity is influenced by genetic and epigenetic

factors. This article shows the need for more research to be made in order to know more on the mechanisms influencing human longevity.

Finally, the implementation of DTC tests as well as the utility of findings raises a host of ethical issues. The returning of findings, particularly incidental findings, is controversial and highly debated. Lucivero and Prainsack offer an interesting perspective on these issues in their discussion of the 'lifestylization' of health. In concert, they, Clift et al. and Pavlidis et al., discuss ethical complexities of result returning, including incidental findings, in different clinical contexts and to different types of patients. Which results ought a health professional return to the patients, or which patients? Given that not all patients are equally prepared to receive results regarding life-threatening conditions, what type of clinical standard ought to exist? Can professionals truly anticipate how patients and their relatives will be affected by incidental results? How ought clinicians handle these complexities?

In sum, this issue illustrates that genomic progress generates answers but also questions. Deciding whether we know enough to apply what we know is understandably challenging. Medicine, as William Osler so famously said, is a science of uncertainty.<sup>3</sup>

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<sup>2</sup> <http://nutrigenomics.ucdavis.edu/?page=information/Glossary>.

<sup>3</sup> Computers in biomedical research (1965) by Ralph W. Stacy, p. 320.