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Editorial

Utility of Independent Investigators in the Genomics Revolution

Joseph W. Landry*

From the Department of Human and Molecular Genetics, VCU Institute of Molecular Medicine, Massey Cancer Center, Virginia Commonwealth University School of Medicine, Richmond, Virginia 23298, USA

***Corresponding author**

Joseph Landry, PhD, Assistant Professor, Department of Human and Molecular Genetics VCU Institute of Molecular Medicine, Virginia Commonwealth University School of Medicine, 401 College Street Goodwin Labs, Room 167, P.O. Box 980035, Richmond, VA 23298, USA, Phone: (804) 628-1944; Fax: (804) 827-0810; Email: jwlandry2@vcu.edu

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It is with great pleasure that we bring forward JSM Genetics and Genomics as a premiere open access online journal dedicated to publishing high impact manuscripts in the field of genetics and genomics. The launch of JSM Genetics and Genomics could not come at a better time. The field of genetics has exploded in the last two decades, largely due to reduced costs of DNA sequencing. Today, a single 2 week sequencing run from a modern high throughput sequencing machine can generate more data than the combined yearly output of a sequencing center a decade ago. This massive increase in capability has cut the cost of sequencing a human genome from ~$100 million in 2001 to ~$2-3 thousand today [1]. While sequencing costs have come down, participating in this specialized field requires considerable sequencing, computational, and bioinformatics core resources – prohibiting its use to only well-funded investigators. However, as genomics becomes main stream, and as national funding agencies are requiring comprehensive approaches, most geneticists may wonder if there is a place for them in this post genomics world.

The genomics revolution started with the initiative to sequence the genomes of prokaryotes and single cell eukaryotes [2,3]. In each case, soon after the sequence of the genome was released, the research community quickly capitalized on the information to seed ever sophisticated studies. What was once a black box, the genome sequence of their model organism, suddenly became publically available. The sequencing of these comparatively small genomes vetted the technology necessary for the sequencing more substantial genomes, including the sequencing of the mouse and ultimately the human genome [4,5]. At the completion of the human genome project the true scope of what it means to be human had finally come into focus. The realization that humans have similar numbers of genes as flies and worms, reinforced that we do not understand what it is to be human at a molecular level. Subsequent projects like ENCODE (Encyclopedia of DNA Elements), modENCODE, GENCODE (Encyclopedia of Gene and Gene Variants), Functional Analysis Program, and others set out to identify the functional DNA elements genome-wide [6-9]. As a result of these initiatives, we discovered that much of the human genome has a function in at least one of the cell types investigated. These studies suggested that much of what we thought of as useless intergenic DNA encodes functional elements. Case in point, many more noncoding RNAs were discovered than anticipated. These include small regulatory RNAs, long noncoding RNAs, and pseudo genes. In addition to diversity in regulatory RNAs, coding genes were discovered to be commonly alternatively spliced. This transcript diversity, in the context with the myriad of post translational modifications, proteolytic processing, and allosteric changes at the protein level, allows the human genome to encode a large diversity of functional gene products with a relatively small number of genes.

The ability to sequence genomes with frequency allows us to identify genetic variants in the human population. Identifying these variants is the first step forward in understanding how they could contribute to human disease, our variable response to medical treatments, and possibly provide clues to our evolution. Many of these variants are single nucleotide polymorphasusms (SNPs) or small insertions or deletions. High frequency variants were identified through SNP initiatives [10]. Larger scale endeavors like the International HapMap project provided sufficient sequence depth, and DNA from enough individuals, to allow the detection of lower frequency SNPs [11]. Large SNP data bases, and the associated haplotypes, made GWAS studies more tractable, which began to attach molecular causes to complex diseases. Successes identifying variants important for prostate cancer and bipolar disorder were quickly realized as successes of these studies [12,13]. While the successes have been slow, these approaches show great promise in helping us identify the molecular causes for human disease. More aggressive projects like the 1000 Genomes Project, Genetic Variation Program, Centers for Mendelian Genetics, and The Cancer Genome Atlas will serve to greatly expand or understanding of the contributions of mutation and variants have in human disease, and phenotypic variation [14,15].

The individual investigator can feel removed from the discovery process while these advances are occurring at a genome wide scale. Certainly, for most investigators such as me, it is unrealistic to consider proposing large scale genome wide studies. While the costs and required infrastructure are prohibitive for large scale projects, small scale studies on

individual proteins/RNAs are readily achievable at all universities. Many of the required resources for performing these studies are available as complete kits from reputable suppliers, and much of the software for data analysis is available as open source. Once obtained, in-house data sets can be compared to those from the larger consortiums using user friendly genome browsers like UCSC Genome Browser or more sophisticated tools like Galaxy [16,17]. Through these genome wide analyses, relationships can be discovered with much greater significance than traditional studies using limited regions. Once a genome wide relationship is established, specific studies can be carried out, focusing in on individual targets. These studies have traditionally been investigator driven labor intensive endeavors, and will likely be for the foreseeable future, largely because the functions of many gene products are context specific. It is with a combination of both traditional genetics, and those at the genome wide scale, can individual investigators make significant contributions to their specific areas of study.

For the first time, individual investigators have access to comprehensive data sets with which to plan future studies. Access to these data sets, and the ability to generate them in house, has greatly strengthened the discovery tools of the individual investigator. It is over this backdrop that JSM Genetics and Genomics is launched. With an emphasis on individual investigator driven initiatives, JSM Genetics and Genomics seeks to publish quality work, with special interest in those who can marry traditional and genome wide approaches. Any area of genetics will be seriously considered by the Editorial Board for peer-review. Preference for Original Submissions will be given to manuscripts delineating genetic mechanism, rather than those with descriptive observations. In addition JSM Genetics and Genomics will solicit; Short Reports succinctly describing an important observation in genetics, Review Articles describing current trends, and Case Reports which extend the field of medical genetics. And through these venues, we will provide a quality resource to the individual investigator of the genetics community.

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