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Personalized- and One- Medicine: Bioinformatics Foundation in Health and its Economic Feasibility

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Personalized medicine's foundation rests on the use of molecular technologies, which are being used to identify genetic mutations, polymorphisms, and variants that can be associated with an individual's genetic make up, revealing risk factors and predictive data. Needless to say this same analysis can be performed on various types of cancers, including samples stored for many years under the right conditions. For the most part, these technologies employ microarray and RNA-Seq methodologies, which examine large numbers of gene expressions at a time, providing clustering and patterns of this expression. The methodologies and their evaluative outcomes further demonstrate that more than a single gene is involved with various phenomena. However, given the mass of data emerging from this analysis, and commonalities they reveal between various phenomena/disorders, achieving 100% certainty may not be that easy. Another outcome from this massive store of molecular data is the concept of one medicine. This field has been developed by researchers in a variety of disciplines (e.g., medical and veterinary science) that advocate for greater integration of animal and human health. One medicine takes advantage of the fact that molecular commonalities in major biochemical pathways occur because of evolutionary conservation, which is dependent on stereospecificity. In this regard, the foci of personalized medicine and one medicine are quite broad and require trained professionals, as well as a lowering of cost in order to be better integrated into mainstream medical practice.

MeSH Keywords: Individualized Medicine • Economics

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Background

Throughout human history we have sought to understand illness as a means of relieving its symptoms, particularly with respect to devising treatment options in the hope of developing cures. In this pursuit of medical knowledge we have shifted the balance of our answers and beliefs from non-evidence based phenomenology to one that is evidenced based. In this regard, it is recognized that placebo and 'folkloric', or traditional, types of intervention do take place through to today. Also present in this multi-layered complex of curing are the understandings that physical resources are required for treatments, new discoveries are ongoing, and old methodologies undergo scrutiny. The technologies available today for improving symptoms and enhancing the chances of finding rapid cures/treatments now offer opportunities for advancing empirical knowledge, especially into the realm of personalized medicine whereby target therapies will provide for more precise outcomes on an individual basis. Nonetheless, ethical concerns must be taken into account since denial of determinations/advanced knowledge based treatments associated with novel technologies may be dependent on issues of access, as well as the availability of financial resources. Thus, it is evident that our understandings of molecular biology have brought us both medical optimism and significant concerns.

Understanding the control of gene expression is critical for our understanding of the relationship between genotype and phenotype[1–4]. The need for reliable assessment of transcript abundance in biological samples has driven researchers to develop novel technologies, such as DNA microarray and RNA-Seq. Briefly, the differences between the knowledge gained and methods used become apparent once the target sequences go beyond known genomic sequences and, thereby, increasing information [5]. Indeed, the depth of this potential information is necessary for the development of personalized medicine. Furthermore, due to phenoconversion, giving attention solely to genotype may miss clinical outcomes, signaling the need for caution in data interpretation [6].

Discussion

The microarray and RNA-Seq techniques are somewhat different, providing an abundance of information requiring explanation. Hybridization-based techniques such as microarray rely on and are limited to the transcripts bound to the array slides. Microarrays are only as good as the bioinformatics data available for the model organism's genome and transcriptome. While RNA-Seq detects annotated transcripts, it will also detect novel sequences and splice variants. RNA-Seq can use data from the same experiment to detect non-coding RNA, single nucleotide polymorphisms, and fusion genes, as well as characterize exon junctions. The utility of RNA-Seq for other bioinformatics studies aside from gene expression profiling far exceeds that of a microarray. In this light, RNA-Seq is useful for distinguishing host from parasite transcripts, studying symbioses, and examining transcripts from non-model organisms, including bacteria [5]. Analysis of RNA-Seq data also requires extensive experience and the bioinformatics skills necessary to process the data files. The data analysis techniques not only differ in the type of software used to initially reduce the data sets [7], but also for each use of RNA-Seq [8,9]. For example, the size of an average raw data file from an Agilent microarray is 0.7 MB, while the normal size of uncompressed RNA-Seq raw file is approximately 5GB. Thus, for just one study, these techniques generate an enormous amount of data, parts of which remain to be interpreted, particularly with respect to patterning and clustering of gene expression. This bioinformatics-based technology illustrates the growing need for physician and technician training and greater research into interpretational discoveries. This is especially significant due to the fact that it will eventually enter into the realm of clinical decision-making, once government approvals for such technologies are reached.

In recent years the field of full genome sequencing has been growing at a healthy pace. Today's knowledge of traits associated with genome pathology is made by inference from common traits without taking greater advantage of the knowledge gained in large sample studies, with demonstrate rare variations in the overall pool of populations and individuals. These studies have focused on humans [10–13]. Importantly, variants that emerge have not been incorporated in clinical practice, which is noteworthy due to the fact that these genetic variations may be the very foundation of personalized medicine and may also be used in revealing an organism's evolutionary history. As this field grows it increases its potential applicability in a wide array of clinical research. As noted earlier, it will assist physicians in making critical medical decisions. At present, however, these technologies are costly and, therefore, their integration into mainstream medical practice is hampered [5]. Nevertheless, as with many technologies, in time the price will decrease so that the information revealed could be readily used to contribute to patient care, including the development of individual databases and their variation, otherwise understood as personalized medicine. As this invaluable technology becomes more economical, it can be argued that there will be better proficiency in understanding genetic phenomena, particularly those involving gene pattern expression, benefiting clinical disciplines and improving the knowledge base of physicians, genetic councilors, and researchers. As such, the use of this broad cache of genome-related information will allow for more effective clinical examination and decision-making, also involving disorder progression and the development of strategic treatment modalities. In this regard,

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gene expression determinations may find similarities in various tumors previously considered different since they were originally described in one type of tissue/organ, whereas now the revealed expression pattern identifies it as similar. The same was found true for proinflammatory processes constituting a commonality in many disorders [14,15].

Moreover, the genetic composition and information obtained from human, animal, and plant populations will become even more important for the novel design and interpretation of disease mapping processes in living organisms. This knowledge will aid in the further development of the concept and phenomenon of one medicine, which combines information in the veterinary and human medical fields. In support of one medicine, there are many health disorders that demonstrate a coupling of disease transmission and occurrence between animals and humans (see [3,16–22]), demonstrating a common molecular substrate between the two. Thus, it is well known and understood that animals can have the same type of disorders found in humans (e.g., cancer, diabetes, arthritis, etc.), making comparative medicine an old discipline [3,16–22].

Given the many genome commonalities, one medicine also becomes important as a means of reducing associated medical costs. This potential can obviously be extended to all living organisms, and the variants can be incorporated into the knowledge base as another critical factor in medicine and evolution. However, we do recognize the fact that between different organisms, variation in the expression of genes will vary just as their biochemistry does as a way to accommodate and adapt to different environments. Thus, counter-intuitively, these variations demonstrate the dynamic character of common life processes to survive. In part, this also explains why some medicines designed on the basis of stereospecificity may be ineffective in different organisms.

As the fields of personalized and one medicine mature, in part, based on this wealth of molecular data, it will be invaluable to be able to correlate the molecular information with individual case reports. Fortunately, what may be emerging is that molecular data can be retro-matched to appropriate patient pathologies. It can be predicted that associations in this analysis will emerge as financial access to the technology improves. In any event, the newness of these technologies and their insights require validation via established methodologies (RT PCR, chromatography, and electrophoresis separation techniques coupled to (mass) spectrometry).

The emerging bioinformatic data and analysis will place one medicine in its proper perspective. For example, it is clear that the metabolic energy pathways are nearly the same or have similar components in all living cells [23]. The same can be true for chemical messenger systems, growth, and development processes. In this regard, specific bioactive components/biochemicals are conserved and enhanced during evolution, as well as being used in novel ways [24–27]. Retention of specific molecules (information) appears to have started before animals and plants split during evolution. The molecular matching identities of these molecules are high, demonstrating that this is not occurring by chance in diverse living organisms. Accordingly, this information has tremendous predictive value for biomedicine that can and will be used in one medicine. It comes as no surprise then to find that pharmaceuticals may affect the same target and/or different processes as demonstrated by adverse reactions reported for a particular drug. These similar molecular commonalities may also explain why different disorders exhibit comorbidities [28].

Furthermore, this concept of one medicine aids in the understanding of why plants can and do produce bio-active chemicals, including signaling molecules of use in intracellular and extracellular communication, that influence animals as both nutrition and/or medicine [29]. The “force”/factor conserving this phenomenon in evolution is stereo-specificity (lock and key-like process), whereby these pathways require multiple conformational-specific enzymes. The enzymes are conformationally linked in specific pathways, constraining new information that may get in the pattern of final product expression [24,25]. This process preserves information, explaining why similar important molecules are found in all animals and in plants (common origin), and can be used in each other’s signaling processes. In addition, conformational matching in a multiple enzyme mediated pathway forces the system to remain the same. In turn, this allows for little novel signal molecule variation across different phyla from single cell organisms to invertebrates and eventually vertebrates, expressing the critical genes in highly developed cellular network, finally allowing for cognition [24,26,27,30,31]. In this light, given common signal molecules, the latest evolutionary advance occurs in intercellular signaling and the pattern of cellular organization, e.g., networking. Variation in the critical signaling/ pathway molecules will only be tolerated if one step exhibits conformational homologies with the existing pattern of processing, producing a related but distinct product (e.g., catecholamine synthesis [24,26,27,30,31]). Taken together, one medicine becomes very feasible and based on sound molecular/cellular and intercellular networks that are similar across living organisms. This provides for the use of similar strategies, dealing with pathological issues [28] in all animals and, in some instances, plants since they are part of a common core of life.

Conclusions

Given the advances in genome and gene expression technologies, an enormous amount of information is generated that

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enable the biomedical community to make strides toward the development of personalized medicine. In this regard, once informational analysis processes mature and, in part, computational biology and the technology becomes increasingly economical, medical costs will decrease as a result of more precise treatment modalities. Moreover, these treatment modalities will be developed based on specific target design and at a more rapid pace. This development will be assisted by the realization that common polymorphisms and gene variants reveal their significance and, thereby, this can be incorporated into the medical therapy regime for individuals, thus improving the treatment efficacy. An additional factor that can help to decrease medical costs is one medicine. Common signaling processes are abundant in living organisms, demonstrating a high level of conservation during evolution. This phenomenon can be exploited, such as though the development of drugs for one organism that can be used in another for the same, or different reason. A single drug may have influences that are regarded as healthy across species lines, making their testing and further development more economical and, thereby, lowering costs.

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