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Pharmacogenetics and the Future of Perzonalized Medications

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Abstract

Clinical genetic testing has grown across the globe over the past 30 decades as the causative mutations for Mendelian diseases have been pointed out, especially helped in part by the recent advances in molecular technologies. Substantially, the use of up to date tests and other strategies such as diagnostic confirmation, testing prenatally, and population-based carrier screening is offered with caution and careful consideration before implementing clinically. This may facilitate the appropriate use of brand new genetic tests available. Even though the field of pharmacogenetics began in the early 50s, clinical testing for the fundamental pharmacogenetic variants implicated in inter-discrete drug response variability has become available only recently. It helps clinicians to judge and prescribe drugs more wisely. Nowadays, most of the health organizations and drug safety commissions provide revisions that include pharmacogenetic information leaflets for selected drugs. However, regardless of some pharmacogenetic associations with adverse results, rest of the proposals has been proven successfully. When compared with testing for the Mendelian diseases, pharmacogenetic testing for other manifestations may have only a negligible positive predictive value, which is one rationale for underutilization. A number of other barriers remain with implementing clinical pharmacogenetics, including lack of clinical utility, professional education, and regulatory and reimbursement issues, among others. Through this review we put forward some of the challenges and barriers faced in executing a clinical pharmacogenetic test.

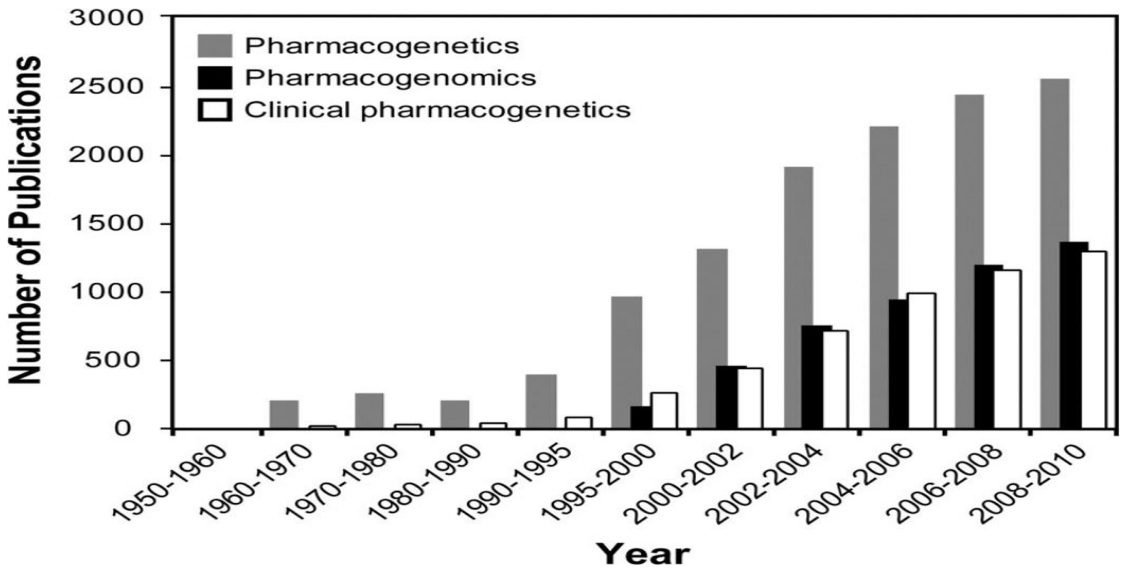
Keywords: *pharmacogenetics, healthcare, omic, medicine*

EVOLUTION OF GENOMICS AND PERSONALIZED MEDICINE

The notion of "personalized medicine" was proposed in the 1800s by Sir William Osler, a physician from Canada. It was he, who noted a great variability among individuals. Nevertheless, a brand new definition has come up to assimilate personal genetic information into a patient's provisional assessment and past medical history to implement a successful medical management. The important fields of applied research in this sector include the identification of genetic basis of some common diseases, learning how the genes and the surroundings interact to give origin to human diseases , and using the biomarkers (pharmacogenetic) to provide much effective pharmacological therapy. Even though interpreting the genetic benefaction to disease is far from being perfect, thousands of "normal" DNA variants have been incorporated with diseases along with phenotypic traits; and many companies have exploited this information to offer DNA-based testing that puts ray of hope into personal traits and risks for diseases spellbindingly. Various risk calculation methods and choices of genetic markers have resulted in discrepant results, when contrasted against each other and this issue needs to be addressed, perhaps with more research.

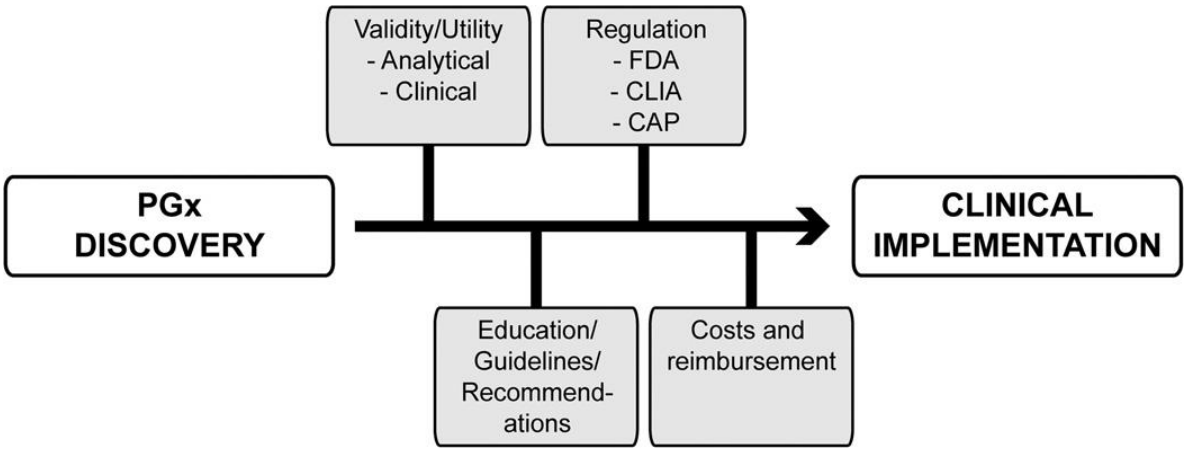
Pharmacogenetics has grown as one of the prominent and potentially most actionable sectors of the cadre called personalized medicine paradigm, as witnessed by the hype in the availability of clinical pharmacogenetic testing among CLIA-approved laboratories over the recent years. In contrast, CLIA-approved clinical labs do not conventionally offer testing for variant alleles associated with complex diseases to estimate personal risk. Many excellent reviews have been dedicated to personalized medicine and the potential of pharmacogenetics. More than that, tallying the exponential growth on literature over the past 10 years in applied pharmacogenetics the practice recommendations have been made, with which included a strong endorsement to assimilate as many information as possible, which most DTC companies now do. This was recently been acknowledged by the US FDA with a revision on drug label to include important pharmacogenetic information and in addition to this, stated a commentary on clinical execution and drug development programs.

Thus, practice recommendations have been made, which included a strong endorsement to incorporate as many informative pharmacogenetic markers as possible, which most DTC companies now do.



CLINICAL PHARMACOGENETICS AND IMPLEMENTATION

First and foremost, pharmacogenetic discoveries are often followed by discussions on clinical implementation. However, the identification of genetic markers related with drug response will not always stand to clinically useful predictors of adverse results, and self-reliant replication of genotype-phenotype association is always needed before the clinical implementation. So many of the personalized medicine programs have seeded in clinical pharmacogenetics and its implementation as a logical first step to incorporate genetics and genomics into way more routine and discrete healthcare. In spite of the enthusiasm, each and every one will not be supportive, as shown by the relatively slow physician uptake of available pharmacogenetic tests. The factors which are likely responsible for this, main challenges and barriers for implementation of clinical pharmacogenetics are discussed below.



IN THE UPCOMING ERA

The things to tackle for effective adoption of pharmacogenetics are considerable. Clinicians need to be aware about it, reimbursement should be worked out, and the medical science needs to get behind it. Nevertheless, the future of pharmacogenetics is very much promising. Research networks are forming to support the use of pharmacogenetics in clinical practice. The Vanderbilt University is piloting the Bio-Vu project, in which DNA and genotype data of the patients are being stored and matched to the electronic clinical records. This kind of projects not only provide clinically useful info about the recent state of the art of pharmacogenetics, but also help in disseminating up to date information about relationship between genotype and phenotype. The emergence of 'omic' sciences, Pharmacogenetics and pharmacogenomics, are part of a larger group of "omic" sciences. The suffix "-omics" stands for a larger, much more holistic view and it is being applied to a number of fields—for example, the proteomics(the study of proteins)and the metabolomics(the study of metabolites). Profiling proteins and metabolites delivers vast and vernacular information on a patient that can be clustered, using pattern-recognition software, into population subgroups. The Patterns of multiple proteins or metabolites are extracted from this spectral data to identify disease or response to treatment (pharmacometabolomics). Metabolomics has been shown to predict the response to statins, diagnose myocardial infarction and reclassify cardiovascular risk status. In addition, whereas traditional laboratory chemistry is reductionist, using single biomarkers for single-disease diagnosis, "omic" technologies hold the potential to reveal information on a number of possible

healths or disease states. The type of analytical software that uses "natural language processing" is being applied to clinician-generated notes for deriving new observations and associations between genetic variants and clinical phenotypes. Integrating this information in real-time decision-support modules in the e- health record provides a feedback loop for a rapid assimilation of new knowledge. The identification of "healthy" profiles using these methods can potentially provide a good positive feedback to patients who are undertaking lifestyle changes and treatment. Another fact is that the instrument costs for proteomic and metabolomic profiling are relatively high. However, the ongoing running costs are minimal, estimated at as low as less than $13 per test, as there are no costly reagents. High-volume testing therefore becomes very cost-effective. Although omic science appears futuristic, proteomics and metabolomics are already used in many clinical laboratories to rapidly identify bacteria. These methods have already revolutionized the way laboratories identify microbes, since they are automated, reduce workload, and give very fast results.

Critics of pharmacogenetics claim that the probability of predictive value of genetic testing is very poor, sice it is lacking evidences, and that the expenses are very high. In almost every brand-new technology, the primary result will be coarse, but performance improves day by day with regular use. The major barrier to overcome is adoption. The projects like Bio-Vu are establishing their infrastructure for a feedback loop to swiftly improve upon the status quo and provide the evidence base clinicians demand. The expense of genetic testing is falling rapidly, with a whole-genome sequencing and annotation now costing less than $5,000. The starting range of a pharmacogenetic test can be as low as $100 using low-cost nanotechnology, and the test needs to be performed only once in a patient's lifetime as other related molecular technologies such as proteomics and metabolomics become available and are integrated with genomics, the predictive ability of this technique will improve.

In India, genetics based medication and genetic testing is flourishing day by day, the following institutions are the centers of excellence in pharmacogenetics

1. Genetics and mental retardation clinic, department of paediatrics, AIIMS New Delhi,
2. Genetics cell, Sri Ramachandra Medical College, porur, Chennai.
3. Genetics department, Manipal hospital, Karnataka.

CONCLUSION

Over the last decade there has been a trend away from "one size fits all" to customized "markets of one" in everything from consumer products to education to medicine. Mass customizing, also known as personalization, has been embraced by the internet community as a means to increase efficiency and reduce cost. This occurs by eliminating waste in redundant work or production of ineffective products. Personalization on the Internet has been enabled through the use of informatics, mathematics, and supercomputing. The same tools that have personalized the delivery of consumer products are also being applied to the field of pharmacogenetics. Applied in an evidence based fashion, these new technologies should profoundly improve patient care now and in the future.

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