Example of personalized medicines and respiratory disease biomarkers and pharmaco...

Science, Genetics

Pharmacogenomics alternatively referred to as pharmacogenetics in medical literature is a component of personalized medicine. It refers to the study of genetic polymorphisms that in one way or another influence individual response to drugs. Clinical observations on the effects of genetic polymorphism on the pharmacokinetics and pharmacodynamics of drugs were first documented back in the 1950s. Scientific knowledge on genetic variations is therefore the critical foundation on which pharamacogenomics is based. In specific, the knowledge of how variations in the genes responsible for encoding enzymes and proteins are the main pillars of pharamacogenetics (Belle, 2008). Enzymes play a vital role in drug metabolism. Genes also influence the expression of proteins (receptors) on cells and conversely cellular responses to drugs (Ingelman-Sundberg, et al., 2008).

Chronic obstructive pulmonary disease (COPD) is a chronic lung condition which is normally asymptomatic in its initial stages and which produces symptoms like chronic cough and shortness of breath in its later stages. COPD is heterogenous in nature with many phenotypes. The etiology of airway obstruction, the final outcome of COPD is also heterogenous in etiology. Evidence suggests that mutations in certain genes for instance the severe deficiency of α1-antitrypsin contribute to general COPD. In addition, it is proposed that mutations in other SNPs are responsible for some of the other COPD phenotypes (Hersh, 2010; Anchochea, Gomez and Miguel, 2010). Pharmacogenics is therefore a concept that needs to be explored and where appropriate adopted in the management of COPD.

Pharmacogenomics uses molecular methods to identify potential novel

targets during drug trials. The approaches in current use rely on comparing expression profiles at either the protein (proteomics) or RNA (genomics) levels for a given cell or tissue levels following a relevant stimulus. In genomics, RNA extracted from either a cell or tissue is hybridized on parallel arrays and then compared with arrays of sequence-verified clones developed during the human genome project. These arrays are made on glass slides, membranes or chips. For proteomics, cells or tissues from individuals affected and unaffected by disease are used to make protein lysates after which their expression profiles are compared. The standard proteomics model uses two-dimensional gel electrophoresis for the purposes of displaying and selecting proteins whose amount or mobility changes. The proteins are then cored from the gel after which mass spectrometry is used to identify the protein in question. The other approach used combines the previously discussed pharmacogenomic methodologies with classical genetic approaches. This entails comparing expression profiles for novel genes in tissues obtained from people with and without disease. The identified novel gene products are then prioritized by studying the genes that map to areas of potential linkages in the human genome screen developed so far. It is vital to note that the latter approach presumes that the genes targeted by the drug are also involved in the initiation of the disease (Wolf, et al., 2010; Hall, 2002).

Current evidence suggests that case-based approach is the most widely employed clinical approach in pharmacogenomics. In this case, therapy is tailored to the individual client by first conducting genotyping assays so as to identify any variations in gene expression that may influence drug

metabolism as well as predisposition to certain diseases. After careful consideration of the effects of identified genetic variations, the drugs appropriate for the genetic makeup of the specific individual are prescribed. Pharmaceutical companies, in the section on warnings and precautions of their product labeling are also providing information on the effects of their drugs on patients with genetic polymorphisms (William and Howard, 2008; Collins, 2010).

Knowledge of pharmacogenomics can help health practitioners predict with some degree of certainty which patients are at risk for adverse reactions from certain drugs and thereby take appropriate measures to prevent them. In addition, information on single nucleotide polymorphisms especially those that encode enzymes that metabolize drugs or the receptors targeted by the drugs can help physicians choose the most effective drugs for their patients. Further, knowledge of how genetic variations can alter dosages of drug regimens can also guide physicians in determining the optimal therapeutic dose for their patients. Moreover, knowledge on pharmacogenomics will lower the costs of therapeutic trials since it will enable researchers to target their trials to novel patient populations and thus avoid adverse reactions and the need to repeat these trials. Conversely, this will lower the costs of drugs in the markets. In a nutshell therefore, pharmacogenomic will ensure that patients receive individualized, cost effective, efficacious and safe health care (Collins 2010, pp. 2-3; American Medical Association 2011, p. 3). Pharmacists have a vital role to play as far as pharmacogenomics is concerned. For one, those working in drug regulatory bodies have to facilitate the adoption of evaluation systems as well as champion the uptake

of drug trials that embed the knowledge of pharmacogenomics (Newton, Lithgow, Bennett and Farndon, 2007). Further, they have to decipher via research which genetic determinants and which combinations of the more than 50000 human genes and 1. 4 million single nucleotide polymorphisms (SNPs) currently known influence drug metabolism and responses (Johnson, et al., 2008). Kulkarni (2006) posits that in addition to the research role, pharmacists will also serve as clinicians and educators. As clinicians, they will be responsible for recommending and facilitating the provision of therapies individualized to the genetic makeup of clients. As educators, they will be mandated with developing a pedagogical framework that will facilitate the education of future pharmacists on the interpretation, application, delivery, ethical, legal and other aspects of pharmacogenomics.

Bibliography

American Medical Association (AMA), 2011. Pharmacogenomics: Increasing the safety and effectiveness of drug therapy [pdf] Available at: < http://www. ama-assn. org/resources/doc/genetics/pgx-brochure-2011. pdf> [Accessed 8 october, 2011].

Ancochea, J., Gomez, G. T. and Miguel, D. J., 2010. Toward personalized and integrated treatment of patients with COPD. Arch Bronconeumol, [e-journal] 10, Abstract only. Available at: Pubmed. gov database [Accessed 8 October 2011].

Belle, D. J. and Singh, H., 2008. Genetic factors in drug metabolism. Am Fam Physician [e-journal] 77(11) Available through: Pubmed database [Accessed 8 October 2011].

Collins, F. S., 2010. The future of personalized medicine. NIH Medline Plus [e-

journal] 5(1) Available through: Pubmed database [Accessed 8 October 2011].

Hall, I. P., 2002. Pharmacogentics, pharmacogenomics and airway disease. Respiratory Research, 3(10-10. 6) [Online] Available at: < http://respiratory research. com/content/3/1/10#sec3> [Accessed10 October 2011].

Hersh, C. P., 2010. Pharmacogenetics of chronic obstructive pulmonary disease: Challenges and opportunities. Pharmacogenomics [e-journal] 11(2) Available through: Pubmed database [Accessed 8 October 2011].

Ingelman-Sundberg, M., Sim, S. C., Gomez, A., Rodriguez-Antona, C., 2007. Influence of

cytochrome P450 polymorphisms on drug therapies: Pharmacogeneic, pharmacoepigenetic, and clinical aspects. Clin Pharmacol Ther. [e-journal] 116 Available through: Pubmed database [Accessed 8 October 2011].

Johnson, J. A., Bootman, J. L., Evans, E. W., Hudson, R. A., Knoell, D., Simmons, L. and Meyer, S. M., 2008. Pharamacogenomics: A scientific revolution in pharmaceutical sciences and pharmacy practice. American Journal of Pharmaceutical Education [e-journal] 66 (12-15) Available through: Pubmed database [Accessed 8 October 2011].

Kulkarni, S. M., 2006. Pharmacogenomics: A review. Pharmainfo. net, 4(3) [Online] Available at: [Accessed 8 October, 2011].

Newton, R., Lithgow, J., Bennett, C. and Farndon, P., (2007). How will pharmacogenomic impact on pharmacy practice? Birmingham: NHS National Genetics Education and Development Centre.

William, E. E. and Howard, L. M., 2003. Pharmacogenics: Drug disposition, drug targets and side effects. New England Journal of Medicine, [Online]

Available at: < http://www. nejm. org/doi/full/10. 1056/NEJMra020526? HITS=

20&hits= 20&FIRSTINDEX= 0&searchid=

1050430656687_23774&stored_search=&tdate= 4%2F30> [Accessed 8

October 2011].

Wolf, S. J., Bachtiar, M., Wang, J., Sim, T. S., Chong, S. S. and Lee, C. G.,

2011. An update on ABCB1 pharmacogenetics: Insights from a 3D model into

the location and evolutionary conservation of residues corresponding to SNPs

associated with drug pharmacokinetics. The Pharmacogenomics Journal [e-

journal] 11 Available through: Pubmed database [Accessed 8 October 2011].