Ethnic Population Specific Drug Design

Amit K. Maiti*

Genetic epidemiology Unit, ACI, Oklahoma Medical Research Foundation, OK 73104, USA

Chemotherapy is a treatment of disease conditions with chemical compounds that was an obvious end point of most of the biological research until a separate branch launched as ‘gene therapy’ where genetic information could be manipulated for treatment of diseases. However, much promising ‘gene therapy’ field has achieved little success due to various reasons [1,2]. But the traditional chemotherapy field continues to grow and, until now, the most prominent approach for new drug development. The modern chemotherapy started with the generation of recombinant molecules by genetic engineering to use as drugs was pioneered by Boyer (1971) for insulin [3]. After that several hundreds of recombinant molecules such as interleukin, interferon etc were successfully produced and being used as drugs. In the next approach, disease specific genetic and genomic information were used to develop gene specific drugs. Although not many, but the first and most successful rational drug design is Gleevec, developed by Novartis for some leukemia patients against tyrosine kinase using the information of BCR-ABL translocation specific hyperactivation. In the post genomic era vast explosion of disease specific genetic and genomic information lead to emergence of numerous companies and involvement of academia for developing drugs using patient specific genetic signatures. These also led to the formulation of many directions of the field as pharmacogenomics, pharmacogenetics etc.

But the basic problems of chemotherapies remain elusive. Why a particular drug does not respond to everybody or why different individuals respond differently for a same treatment or why apparently similar individuals experience different complications for a same treatment? Most intriguing problem is that after initial response, some individuals get resistance to the drug and the symptoms relapse. The recent evidences suggest that individual genetic signature might play important role for some of these problems. Identification of genetic variation and its association with drug metabolism could indicate the outcome of drug treatment. When lung cancer patients with EGFR mutation were treated with Gifatinib with an EGFR mutation directed drug, some of the patients were resistant. Subsequent genetic analysis showed that these resistant patients tumor have a second mutation in the same EGFR gene that confers resistance to Gifatinib [4]. Similarly, genetic association studies reveal that HLA-DRB genotype is a major determinant of drug-induced liver injury due to fluclaxacillin. Nat Genet 41: 816-819.

Drug resistance seems to be more towards alteration of the physiology of the cell like changes in MDR (multiple drug resistance) activation or ROS (reactive oxygen species) generation in the cell. However, genetic component for ROS management or MDR are also emerging as an influential factor for chemotherapeutic drug resistance [7]. FDA approved approximately 200 drug metabolism and transporter genes are already in considerations for many studies involving drug resistance. However, large scale association studies with these genes and drug metabolisms seem to be extremely important for specifying drug induced resistance or development of other complications and could be initiated for successful chemotherapy.

References


*Corresponding author: Amit K. Maiti, Genetic epidemiology Unit, ACI, Oklahoma Medical Research Foundation OK 73104, USA, Tel: 405 271 8099; Fax: 405 271 2002; E-mail: akmit123@yahoo.com, Amit-maiti@omrf.org

Received February 22, 2012; Accepted February 25, 2012; Published February 28, 2012


Copyright: © 2012 Maiti AK. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.