Pharmaceutical Regulatory Affairs 2012: Personalised medicine: Introduction of genomics, proteomics and metabolomics in novel drug development and therapy - University of Manchester, London

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Abstract

Personalised medicine is a medical model designed to customize drug therapies to individual patients using their distinct characteristics including demographics, medical histories and most importantly their molecular information (genetic, protein and metabolic profile). Current drug development is principally based on epidemiological studies of large cohorts targeting development of so-called blockbuster medicines. This one-size-fits-all model do not account for individual differences in terms of genetics, proteins and metabolites thus may increase cost, adverse drug reactions and contribute to drug development failure in large clinical trials. Novel drug development and therapy should be based on the principal philosophy of every patient has a unique biology and pathophysiology that should be reflected in the choice of pharmacotherapy, thus resulting in an improved treatment outcome. Recent advances in genetic testing (genomics) have unveiled the potential relations between genetics and diseases. However, this method did not take into consideration of functional and environmental aspects which also play major roles in determining individual differences to clinical outcome. These aspects could be investigated and determined by techniques such as proteomic and metabolomic profiling. Proteomics, through techniques including isotope coded affinity tags, stable isotopic labeling by amino acids in cell culture, isobaric tags for relative and absolute quantification, multidirectional protein identification technology, activity-based probes, protein/peptide arrays, phage displays and two-hybrid systems is utilized in multiple areas through the drug development pipeline including target and lead identification, compound optimization, throughout the clinical trials process and after market analysis. Metabolomics, although the most recent and least developed of the three 'omics considered in this review, provides a significant contribution to drug development through systems biology approaches. Already implemented to some degree in the drug-discovery industry and used in applications spanning target identification through to toxicological analysis, metabolic network understanding is essential in generating future discoveries Molecular information obtained from these analyses may lead to a more targeted drug development strategy and therefore may reduce/prevent drug failure, cost and adverse drug reactions. Through these methods, hopefully the practice of theranostics, a diagnostic test that identifies patients most likely to be helped or harmed by a new medication, will be widely established. The optimization of drug therapy according to the personal characteristics of patients is a perspective direction in modern medicine. One of the possible ways to achieve such personalization is through the application of "omics" technologies, including current, promising metabolomics methods. This review demonstrates that the analysis of pre-dose metabolite biofluid profiles allows clinicians to predict the effectiveness of a selected drug treatment for a given individual. In the review, it is also shown that the monitoring of post-dose metabolite profiles could allow clinicians to evaluate drug efficiency, the reaction of the host to the treatment, and the outcome of the therapy. A comparative description of pharmacotherapy personalization (pharmacogenomics, pharmacoproteomics, and therapeutic drug monitoring) and personalization based on the analysis of metabolite profiles for biofluids (pharmacometabolomics) is also provided. Besides that, these techniques may also provide a platform for preventative drug development strategy in future.