SOCIÉTÉ CHIMIQUE DE GENÈVE

Targeting and individualizing drug treatment: Bioanalytical approaches for personalized medicine

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There are an increasing effort at getting better and more secure use of drugs by increasing our understanding of the existing link between drug's pharmacokinetics (its fate in the body) and pharmacogenetics (genetic traits that influence drug disposition) and the response (or absence of response) and/or the toxicity elicited by drug treatment. In that context, it has been established over the last decades that the therapeutic use of some drugs could be optimized by an individualization of their dosage, based on blood concentrations measurement. This feedback strategy, termed Therapeutic Drug Monitoring (TDM) is now current practice for antiepileptics, immunosuppressant drugs, anti-HIV and antifungal drugs, for some antibiotics drugs, and more recently, for new anticancer targeted drugs. TDM is generally considered for drugs with large inter-individual but limited intra-individual pharmacokinetic variability, with both consistent concentration-efficacy (and concentration-toxicity) relationships. Drug pharmacokinetics is the final phenotypic trait of patient's drug exposure and is influenced by complex genetic and non-genetic factors affecting drug transport and metabolism in the body. Overall, TDM is now considered in case of therapeutic failure, adverse drug reactions, drug interactions problems, doubt on patient's compliance and in several special clinical conditions (pregnancy, pediatrics, hepatic and renal failure, Intensive Care Unit, etc). To that endeavour, the technique of chromatography coupled to tandem mass spectrometry has become an essential component for the development of high throughput multiplex assays to respond efficiently to the increasing number of analytical demands and their application for the TDM of current and new classes of anti-HIV drugs, antifungals, antibiotics and targeted anticancer agents, as well as new antimalarial combinations regimens. In conclusion, current analytical research efforts aim at increasing our current understanding of the complex gene-environmental interplay influencing toxicity and efficacy of pharmacological treatments in patients, thus offering new possibilities for improving the short- and long- term tolerability and response to treatments.

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