CANCER PHARMACOGENOMICS

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An important cause for individual variations in the response and tolerance to drug treatment is the genetic make-up of patients. These variations are often due to germline mutations in genes that encode for drug metabolizing enzymes, transporters, cellular targets and signalling pathways. An important distinction between pharmacogenetics in oncology and other therapeutic fields is that somatic mutations, frequently acquired in cancer tissues, also contribute to the variations in treatment outcome and could fortuitously be exploited in targeted therapy to maximize treatment efficacy. The application of pharmacogenetic testing in cancer therapy has been particularly attractive because of the narrow therapeutic index of chemotherapeutic agents. This talk aims to provide an update on the genetic basis for interindividual variations in therapeutic outcome relevant to key classes of anticancer agents and the potential application of pharmacogenetic in the treatment of cancer. Pharmacogenetic predisposition to severe toxicity will be explained by the examples of irinotecan and 6-mercaptopurine for colorectal and acute lymphoblastic leukaemia patients, respectively. Pharmacogenetic predictors of response will be also discussed, and EGFR inhibitors and fluoropyrimidines (for non-small cell lung and colorectal camcer, respectively) will be used as examples.

Issues of ethnic diversity, use of pharmacogenetic biomarkers in drug development in oncology, and use of germ line vs. tumor DNA will be also discussed.