

IN THIS ISSUE

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Challenges of recording phenotype

The article by Nadkarni (pages 8–10) discusses how individual phenotypic parameters in a data set must be adequately described in order to be comprehensible and minimize the possibility of misinterpretation, and how even the nature of these descriptors depends on the broad category of phenotype that one is describing. The authors then consider the requirements of software tools to assist submission of phenotypic data to an electronic repository, and the means by which standardization of such software could be facilitated.

Current aspects on pharmacogenetics

Although impressive literature documents both a strong participation of genetics in the etiology of attention-deficit/hyperactivity disorder (ADHD) and a high rate of response to stimulants, surprisingly few studies on pharmacogenetics of ADHD have been conducted so far. The article by Rohde *et al* (pages 11–13) reviews two studies that add to the compelling literature indicating the role of DAT1 gene variability in the response to stimulants.

Pharmacogenetics: the ethical issues

Lipton's article (pages 14–16) covers the consultation document issued by The Nuffield Council on Bioethics on

ethical issues raised by developments in pharmacogenetics. The potential of using pharmacogenetics information to improve the efficacy and safety of prescribing medicines is clear. Some have even made the optimistic claim that personalised medicine—'the right medicine, for the right patient, at the right dose'—will only be a matter of time. But both research in pharmacogenetics and its applications raise ethical, legal, social and regulatory issues, which must be considered as this field rapidly evolves.

Sequence variations in the UGT2B7 gene

The article by Holthe *et al* (pages 17–26) presents sequence variation data in the coding and regulatory regions of the UDP-glucuronosyltransferase 2B7 gene (*UGT2B7*) from a cohort of 239 Norwegian cancer patients, and analyses the impact of gene variants on morphine glucuronidation *in vivo*. Their results suggest that factors other than *UGT2B7* polymorphism may influence the variability of morphine glucuronide to morphine serum ratios.

Microarray analysis of the PFC in cocaine abusers

A hallmark feature of drugs of abuse, such as the psychostimulant cocaine (COC), is to alter the expression of a wide array of behavioral, neurochemical, and cellular parameters. It appears that most of the changes seen in mRNA and protein expression as well as biochemical parameters disappear rapidly when drug is discontinued, and may even be blunted by chronic drug exposure. The present study by Lehrmann *et al*

(pages 27–40) employs complementary DNA (cDNA) microarrays to analyze differences in transcription patterns in the dlPFC of seven individual sets of gender-, age- and postmortem-interval-matched COC abusers and controls (CTRs).

Gene expression in cd₄-treated rats

The study by Young *et al* (pages 41–52) utilizes a new ADME Rat Expression Bioarray, containing 1040 metabolism- and toxicology-linked genes, to monitor gene expression from the livers of rats treated with carbon tetrachloride (CCl₄).

Histopathological analysis, hierarchical clustering methods, and gene expression profiling are compared between the control and CCl₄-treated animals. A total of 44 transcripts were found to be altered in response to the hepatotoxin, 19 of which were upregulated and 25 were downregulated.

Polymorphic CYP2B6 in cyclophosphamide bioactivation

The role of polymorphic CYP2B6 in cyclophosphamide (CPA) bioactivation was investigated in human liver microsomes. A total of 67 human liver specimens were first genotyped with respect to the CYP2B6*5 and CYP2B6*6 variant alleles. CYP2B6 apoprotein levels in 55 liver microsomal preparations. The results by Xie *et al* (pages 53–61) demonstrate that the polymorphic CYP2B6 is a major enzyme in the bioactivation of CPA. Moreover, the authors identified a strong impact of CYP2B6*6 on CPA 4-hydroxylation.