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The confidentiality maze in pharmacogenomics

If the public is to fully reap the benefits of pharmacogenomics, policy makers must learn to recognize the specificity of this type of research. Established ethical principles demand that data banks and samples be protected, but guidelines for confidentiality levels ought to reflect and correspond to the reality and needs of productive research. In this EELS paper, Joly *et al* (pp 2–5) propose points of consideration for researchers and IRBs to determine appropriate levels of protection of genetic data in pharmacogenomics research.

Genetic polymorphisms of CYP2D6

Cytochrome P450 2D6 (CYP2D6) plays a central role in human drug metabolism, affecting the metabolism of 20–25% of clinically used drugs. Moreover, polymorphism of CYP2D6 significantly affects the pharmacokinetics of nearly 50% of drugs in clinical use, often resulting in adverse reactions or no response at all. Ingelman–Sundberg (pp 6–13) contextualizes these findings with this comprehensive review of the CYP2D6 polymorphism and its clinical impact, paying particular attention to the evolutionary and functional aspects that may give rise to interethnic differences.

Renin–angiotensin system (RAS) gene polymorphisms

Investigation of the genetic etiology of hypertension has resulted in greater knowledge of the mechanisms involved in the development of high blood pressure and hypertension-induced organ damage. Previous studies have focused on polymorphisms of candidate genes coding for the RAS, which plays an essential role in the regulation of blood volume, arterial pressure, cardiac and vascular function. Furthering this aim, Redon and co-workers (pp 14–20) evaluate the impact of four RAS gene polymorphisms on antihypertensive response and the development of microalbuminuria in patients receiving the angiotensin II receptor blocker telmisartan.

DRD2 genotype and smoking cessation

Despite treatment advances on the front of pharmacologic treatments for smoking cessa-

tion, relapse after successful intervention occurs in a number of patients. To account for this, Swan *et al* (pp 21–29) look to the A1 allele of the dopamine D2 receptor (DRD2) gene, which is associated with the increased likelihood of substance abuse and addictive behavior. In the first large-scale pharmacogenetic study conducted outside of a clinical efficacy trial, the authors investigate whether variants in the DRD2 receptor gene are associated with smoking cessation outcomes following treatment with a combination of bupropion SR and behavioral counseling.

EGR2, PGR variants and lipid levels

Sex steroid hormones have multiple effects on lipid metabolism. In this article, Almeida *et al* (pp 30–34) explore the association of two common SNPs of the estrogen receptor 2 (ESR2) gene and the PROGINS polymorphism of the progesterone receptor (PGR) gene with lipoprotein levels in women of differing hormonal statuses. Using profiles of pre- and postmenopausal women exposed or unexposed to hormone replacement therapy, the authors aim to verify whether levels of serum total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol and triglycerides are influenced by genetic variations according to hormonal status.

IMPA2, bipolar disorder and lithium response

The pathophysiology of bipolar affective disorder is unknown; the only insights into the illness have been won indirectly, from investigations into the mechanisms of drugs used in its treatment. Lithium is the most effective of mood-stabilizing drugs in the treatment of bipolar disorder, and is thought to work by blocking inositol phosphatases within excessively stimulated neurons. Myo-inositol monophosphatase 2 (IMPA2) codes for an enzyme in the phosphatidyl-inositol system that is inhibited by lithium. Dimitrova *et al* (pp 35–41) consider the hypotheses that variation in IMPA2 increases susceptibility to bipolar disorder and that it confers a differential response to lithium treatment.

CYP2A6 and smoking status in Brazilians

Of the hundreds of chemicals present in tobacco products, nicotine is the primary cause of tobacco dependence. Addicted smokers adjust their smoking to maintain constant nicotine levels in the body, thereby acting against the drug's elimination through

C-oxidation to cotinine. Cytochrome P450 2A6 is the major enzyme catalyzing this reaction, and this catalytic activity displays significant interindividual differences due to polymorphisms within the CYP2A6 gene. Vasconcelos *et al* (pp 42–48) investigate several CYP2A6 polymorphisms and the correlation with smoking habits in Brazilians.

COMT polymorphisms and antidepressant response

The catechol-O-methyltransferase (COMT) is a major degrading enzyme in the metabolic pathways of catecholaminergic neurotransmitters. In this paper, Szegedi *et al* (pp 49–53) investigate whether the functionally relevant Val^{108/158}Met gene variant is associated with differential antidepressant response to mirtazapine and paroxetine in patients with major depression. The authors find that polymorphisms within the COMT gene seem to influence the time course of response and clinical efficacy of mirtazapine, but not paroxetine.

Interethnic variability of ERCC2 polymorphisms

Previous studies have examined excision repair crosscomplementing rodent repair group 2 (ERCC2) and its association with response to platinum therapy, lung cancer risk and DNA repair capacity. Owing to its importance in DNA damage control, variability in ERCC2 expression and function have a serious impact. King *et al* (pp 54–59) examine ERCC2 polymorphisms and haplotype structure among African, Asian and European population groups. Finding significant differences in haplotype structure and frequency between populations, the authors expect that this information on ERCC2 genomic structure will facilitate the construction of definitive studies to clarify the clinical role of this gene.

CYP1A2 association with Tardive Dyskinesia

Tardive Dyskinesia (TD), an iatrogenic disorder characterized by repetitive, involuntary movements of the face and limbs, affects approximately 20% of schizophrenia sufferers on long-term treatment with typical antipsychotics. Since CYP1A2 is one of the major genes involved in the metabolism of xenobiotics, study of SNPs in this gene has major pharmacogenetic implications. Tiwari *et al* (pp 60–69) attempt to establish the association, if any exist, of six functional SNPs in CYP1A2 gene with TD in schizophrenic subjects from north India.