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Human tyrosine kinase B neurotrophin receptor gene and AD

Studies have identified multiple chromosomal regions as sources of potential susceptibility to AD and other addictions. For example, cigarette smoking with or without AD was linked to broad regions of chromosomes 9 and 11. Among the candidate addiction susceptibility genes defined were those that encode the neurotrophin, brain-derived neurotrophic factor (BDNF, chromosome 11) and its cognate receptor, neurotrophic tyrosine kinase receptor B (TrkB) (NTRK2, chromosome 9). To identify sequence variants in genes that may have roles in neuronal responses to alcohol, Xu and colleagues re-sequenced the 5′ region of NTRK2 and determined linkage-disequilibrium values and haplotype structure and performed association analyses using 43 single nucleotide polymorphisms covering the entire NTRK2 region in alcohol-dependent subjects with antisocial personality disorder and healthy controls.

Cannabinoid CB2 receptor and alcoholism

The exact mechanism behind alcohol addiction is not completely understood. There appears to be no single gene that plays a significant role in alcoholism and small functional gene effects may act with environmental factors to promote alcoholism. Studies support the role of the endocannabinoid system in alcoholism. In this study, Ishiguro and co-workers studied whether cannabinoid type 2 receptor in the central nervous system plays a role in alcohol abuse/dependence in an animal model and then examined an association between the CB2 gene polymorphism and alcoholism in humans.

Fetal hemoglobin and sickle cell anemia

Fetal hemoglobin (HbF) inhibits the polymerization of sickle hemoglobin. Many complications of sickle cell anemia are associated with the level of HbF, which is inversely associated with mortality. As a result, investigators have tried to find pharmacological means of increasing HbF production. Hydroxyurea is one drug that increases HbF concentration in patients with sickle cell anemia. Most patients respond to hydroxyurea treatment with an increase in HbF. The regulation of HbF level might be a complex genetic trait. In this study, Ma and co-workers hypothesized that single-nucleotide polymorphisms in candidate genes or quantitative trait loci with putative roles in the regulation of HbF production might modulate the HbF response to treatment with hydroxyurea.

Aspirin resistance in Japanese patients

Aspirin prevents the production of thromboxane A2 by irreversibly inhibiting platelet cyclooxygenase, exhibiting antiplatelet actions. This agent has been reported to prevent relapse in patients with ischemic heart disease or cerebral infarction via this mechanism. However, aspirin is not effective in some patients. Furthermore, many studies have investigated the platelet responsiveness to aspirin in Caucasians at the gene level but few studies have been done in Japanese patients or healthy volunteers. In this study, Fujiwara and co-workers evaluated aspirin resistance in Japanese based on the suppressive degree of platelet aggregation before and after aspirin administration.

RFC-1 polymorphism and methotrexate outcome in rheumatoid arthritis

Folate antagonist methotrexate (MTX) is used to treat rheumatoid arthritis. MTX is taken up by cells via the reduced folate carrier (RFC) and then converted within the cells to polyglutamates. Studies have shown that RFC-1 expression may influence the efficacy of MTX. Studies have suggested that G80A polymorphism in RFC-1 is associated with altered folate/antifolate levels and may influence the efficacy of MTX. In this study, Drozdzik and co-workers examined the association between RFC-1 G80A polymorphism and MTX treatment outcome in rheumatoid arthritis patients.

CYP2D6 poor metabolizers and schizophrenia

Cytochrome *P*450 enzyme (CYP2D6) activity is related to personality traits, which suggests that CYP2D6 enzyme may have an endogenous neuroactive substrate or product. The CYP2D6 gene is highly polymorphic, with alleles causing absent poor metabolizers, decreased, normal extensive metabolizers and increased activity ultra-rapid metabolizers owing to the presence of two or more copies of a functional CYP2D6 allele existing in tandem on the same chromosome. Therefore in this study, LLerena and co-workers analyzed the frequency of CYP2D6 poor metabolizers among schizophrenic patients compared to healthy volunteers.

Ethanol and *C. elegans* behaviour

The *C. elegans* genetic model provides a powerful insight into the molecular actions of ethanol through the use of forward genetic screens. Studies show that the behaviour of *C. elegans* in response to alcohol is similar to human behavior. One key issue has been the internal concentration of ethanol following external application of ethanol and how this internal concentration relates to the potency of ethanol in the mammalian nervous system. In this study, Mitchell and co-workers examine this question, which is an important consideration for the further use of *C. elegans* as a model for the study of the intoxicating actions of ethanol.

Catechol-*O*-methyltransferase polymorphisms and schizophrenia

Two recent meta-analyses concluded what the most promising schizophrenia genes at the 22q and 8p regions are the catechol-O-methyltransferase (COMT, 22q11.21) and neuregulin (8p21–p12) genes. COMT catabolizes monoamines in the brain, including dopamine, and studies have implicated dopamine in the development of schizophrenia. In this study, Molero and colleagues tested for an association between a COMT haplotype and schizophrenia-spectrum disorders and for an eventual influence of a specific COMT genotype in the clinical outcome and response to treatment.