News, literature, and events in the ethical, social, and legal implications of psychiatric, neurologic, and behavioral genetics.

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The next Braingenethics Update (Vol. 2, No. 10) will appear in January 2015. Have a wonderful holiday season!

In the Literature

Whole Issue: Molecules and Psychiatry in The American Journal of Psychiatry

The November issue of *The American Journal of Psychiatry* features a number of articles focused on the molecular mechanisms of psychopathology. One article and editorial investigate whether circulating miRNA can serve as a diagnostic biomarker for schizophrenia. The research finds that up-regulation of miR-130b and miR-193a-3p is a

Thinking About CRISPR: Is Eugenics Inherently Bad?

By Erik Parens

If a technology such as CRISPR-Cas9 could be used to safely and effectively treat diseases or create what some see as improvements in future generations, we would have to face the question we didn't need to face back in 1990 when the Human Genome Project was getting off the ground. Even if it won't be

state-independent biomarker for schizophrenia, and that these two miRNAs could be used to develop a diagnostic tool for schizophrenia. Other articles take up the molecular mechanisms of schizophrenia, bipolar disorder, and depression.

A Post-Genomic Surprise: The Molecular Reinscription of Race in Science, Law, and Medicine

By Troy Duster

The completion of the first draft of the Human Genome Map was heralded as the advent of the "Century of Genetics," which was to move medicine beyond racialized thinking and taxonomies of human difference. However, gene therapies turned out to be much more complicated than anticipated, and again, pharmaceutical companies began to focus their efforts on drugs that might be "related" to population differences based upon genetic markers. While the *language* of "personalized medicine" dominated, research on racially and ethnically designated populations' differential responsiveness to drugs dominated the empirical work in the field. This paper explores the implications, in both health and non-health contexts, of genomic research that treats race as empirical data within discursive spaces that tend to see it as socially constructed. A number of responses appeared in the same issue, adding depth and next steps to the conversation.

Interaction Between DRD2 and AKT1 Genetic Variations on Risk of Psychosis in Cannabis Users: a Case–Control Study

By Marco Colizzi et al.

> possible to use this technology to alter the sorts of hugely complex traits – say, intelligence – that are envisioned in sci-fi movies such as Gattaca (1997), it might be possible to use it to edit out some disease traits, especially rare ones that result from mutations in single genes. More ambitiously, perhaps it could be used to edit in some enhancements such as muscles of greater strength or bones of greater length. Whatever the traits, once the fig leaves of safety and efficacy fall away and we have a technology that can alter the traits of future generations, the naked ethical question stares back at us: is eugenics, really, inherently bad?

Defects in tRNA Anticodon Loop 2′-O-Methylation Are Implicated in Nonsyndromic X-Linked Intellectual Disability due to Mutations in FTSJ1

By Michael P. Guy et al.

Mutations in the gene FTSJ1 cause nonsyndromic X-linked intellectual disability (NSXLID), but the role of FTSJ1 in tRNA modification is unknown. This study directly links defective 2'-*O*-methylation of the tRNA anticodon loop to FTSJ1 mutations, suggests that the modification defects cause NSXLID, and may implicate Gm_{34} of $tRNA^{Phe}$ as the critical modification. These results also underscore the widespread conservation of the circuitry for Trm7-dependent anticodon loop modification of eukaryotic $tRNA^{Phe}$.

Impulsive Alcohol-Related Risk-Behavior and Emotional Dysregulation

Genetic factors may explain the differences in individual sensitivity to the psychosis-inducing effects of cannabis. The results of this study indicate a model of interaction known as 'qualitative G×E interaction' with a crossover pattern: carriers of risk allele(s) for one of two genes, compared with individuals carrying no risk alleles, have a lower probability of psychotic disorder if they never used cannabis but a higher probability if they have a history of cannabis use. Similarly, carriers of both the risk alleles have the lowest probability of psychotic disorder if they never used cannabis but the highest probability if they have a history of cannabis use, especially of daily use.

Targeted Next-Generation Sequencing Analysis of 1,000 Individuals with Intellectual Disability

By Detelina Grozeva et al.

This study assesses the value of sequencing a cohort of probands to provide a molecular diagnosis of intellectual disability (ID), without the availability of DNA from both parents for de novo sequence analysis. This modeling is clinically relevant as 28% of all UK families with dependent children are single parent households. To diagnose patients with ID in the absence of parental DNA, study authors recommend investigation of all loss of function variants in known genes that cause ID and assessment of a limited list of proven pathogenic missense variants in these genes.

Among Individuals with a Serotonin 2B Receptor Stop Codon

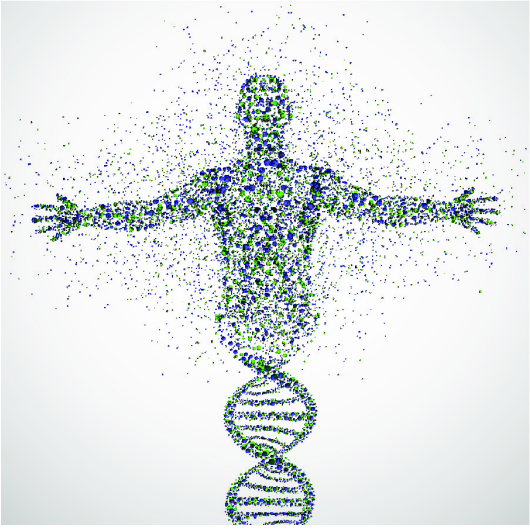
By Roope Tikkanen et al.

A relatively common stop codon associated with impulsivity was identified in a Finnish population. The tridimensional personality questionnaire was then used to measure impulsive and aggressive behavior both while sober and under the influence of alcohol, as well as alcohol consumption. Regression analyses showed that among the HTR2B Q20* carriers, temperamental traits resembled a passive-dependent personality profile, and the presence of this codon predicted impulsive and aggressive behaviors particularly under the influence of alcohol. Results present examples of how one gene may contribute to personality structure and behaviors and how personality may translate into behavior.

Canonical Genetic Signatures of the Adult Human Brain

By Michael Hawrylycz et al.

The authors applied a correlation-based metric called differential stability to assess reproducibility of gene expression patterning across 132 structures in six individual brains, revealing mesoscale genetic organization. The genes with the highest differential stability are highly biologically relevant, with enrichment for brain-related annotations, disease associations, drug targets and literature citations. Genes in neuron-associated compared to non-neuronal networks showed higher preservation between human and mouse; however, many diversely patterned genes displayed marked shifts in regulation between species. Finally, highly consistent transcriptional architecture in neocortex is correlated with resting state functional



[The Mouse That Trolled: The Long and Tortuous History of a Gene Mutation Patent That Became an Expensive Impediment to Alzheimer's Research]

By Tania Bubela, Saurabh Vishnubhakat, and Robert Cook-Deegan

This case study presents a tale of the discovery of a rare mutation for early-onset Alzheimer's disease patented by a sole inventor and licensed to a non-practicing entity (NPE) which then brought costly litigation against 18 different defendants. This article discusses the policy implications of the litigation while questioning the value of patents in the research ecosystem and the role of NPEs ("patent trolls") in biotechnological innovation.

To contribute a news item, an academic article, or an event on the ethical, legal, and social implications of psychiatric, neurological, and behavioral

connectivity, suggesting a link between conserved gene expression and functionally relevant circuitry.

NIH Researchers Link Single Gene Variation to Obesity

A single variation in the gene for brain-derived neurotropic factor (BDNF) may influence obesity in children and adults. This study suggests that a less common version of the BDNF gene may predispose people to obesity by producing lower levels of BDNF protein, a regulator of appetite, in the brain. The authors propose that boosting BDNF protein levels may offer a therapeutic strategy for people with the genetic variation, which tends to occur more frequently in African Americans and Hispanics than in non-Hispanic Caucasians.

In the Media

[Geneticist Craig Venter Helped Sequence the Human Genome, and Now He Wants Yours]

By Carl Zimmer

Craig Venter, who came to prominence in the 1990s with his involvement in the first draft of the human genome, has launched a new company whose flagship product is a $25,000 examination of the human body. It uses two types of genetic sequencing, as well as three dimensional scanning and a battery of blood tests (among others) to, according to Venter, "show the value of actual scientific data that can change people's lives." The project, additionally, will amass an enormous amount of disidentified data about its participants, to be used in various research projects.

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