News, Literature, and Events in Braingenethics

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Braingenethics Update

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Be sure to scroll down for special spotlights on pharmacogenetics, secondary findings, and the Genetics issue of *Current Opinion in Psychology*.

The next Braingenethics Update will appear in mid-December. We will resume our end-of-month schedule for the February issue, coming out late January 2019.

Job Announcement

The Columbia University CEER and The Hastings Center jointly announce the availability of a two-year post-doctoral research position to begin summer 2019. The goal of the position is to develop research skills on the ethical, legal, and social implications (ELSI) of genetics, with a special focus on psychiatric, neurologic, and behavioral genetics. Applicants should have recently completed a terminal degree (e.g., PhD, JD, MD) in the social and behavioral sciences, genetics or other basic sciences, epidemiology, nursing, medicine, law, or one of the humanities. For more information and to apply by December 3, click <u>here</u>.

In the Literature

Return of Results and Data to Study Participants

Susan M. Wolf and Barbara J. Evans A recent report from the National Academies purports to advocate for increased access to data for participants in biospecimen research. However, Wolf and Evans explain, the report's recommendations would introduce major roadblocks for return of results that exceed current barriers.

<u>Standardizing Return of Participant</u> <u>Results</u>

Jeffrey Botkin et al.

The members of the National Academies committee that released recommendations for return of results for subjects in biospecimen research refute Wolf and Evans' claims and express confidence that their recommendations break down many of the existing barriers to the return of results and, if followed, will enhance collaboration among all stakeholders.

Clinical Implications of APOE Genotyping for Late-onset Alzheimer's Disease (LOAD) Risk Estimation: A Review of the Literature

Victoria S. Marshe et al.

Marshe and colleagues review 31 studies that investigated predictive genetic testing for risk of developing late-onset Alzheimer's disease. Positive effects include lifestyle changes, while negative effects include anxiety, depression, and distress. The authors call for the development of a risk assessment tool and more empirical research on the implications of testing.

<u>Clinical Utility of Reinterpreting Previously</u> <u>Reported Genomic Epilepsy Test Results</u>

In the Media

Elizabeth Warren and the Folly of Genetic Ancestry Tests

Alondra Nelson

Elizabeth Warren's test for Native American ancestors illustrates the common conflation of genetics, a set of scientific facts, and identity, a set of social relations.

More Autism Genes Identified

Ashley Yeager

A recent study of over 37,000 individuals with autism identifies 34 new genes relevant to autism's etiology.

The Approach to Predictive Medicine That Is Taking Genomics Research by Storm

Matthew Warren

The genome-wide association study and polygenic risk score stand to revolutionize medicine, but at what cost?

The 'Geno-Economists' Say DNA Can Predict Our Chances of Success

Jacob Ward

"Geno-economists" like Daniel Benjamin and Dalton Conley express excitement about the policy potential of polygenic risk scores. But factors like the scientific focus on white participants' DNA, greater genetic diversity of those with African ancestry, and market forces complicate the success story sociogenomics hopes to tell.

Sociogenomics is Opening a New Door to Eugenics Nathaniel Comfort

Countering the egalitarian vision

for Pediatric Patients

Jeffrey A. SoRelle et al.

Given a finding of high rates of genetic variant reclassification among pediatric patients who underwent genetic testing for epilepsy, SoRelle et al. suggest that results be reinterpreted at least every two years.

Ethical Considerations in Neurogenetic Testing

Xiaowei W. Su and Zachary Simmons Su and Simmons review ethical issues related to genetic testing for neurologic diseases, with a focus on clinical practice.

Risk Perception Before and After Presymptomatic Genetic Testing for Huntington's Disease: Not Always What One Might Expect

Kelsey Stuttgen et al.

Despite the clear genetic etiology of Huntington's disease (HD), over a quarter of patients tested for HD indicated a change in perceived risk opposite their test results. Stuttgen et al. explore why.

Ethical Concerns Regarding Danish Genetic Research

Thomas Birk Kristiansen and Anders Beich

Kristiansen and Beich argue that Danish biobank research, and in particular the iPSYCH2012 study, fails to live up to standards of informed consent and ethical research.

Response to "Ethical Concerns Regarding Danish Genetic Research"

Preben Mortensen

An author of the study criticized by Kristiansen and Beich responds that their ethics standards are well within standards set by Danish and international bodies. forecasted by sociogenomicists, Comfort argues that the pervasive use of polygenic risk scores in everyday life paves the way to a eugenic future. He points out that sociogenomics' predictive, correlative, and inductive nature has powerful—and underappreciated implications.

The Biological Roots of Intelligence

Shawna Williams

New developments in neuroscience, like network analysis, and genetics, like genome-wide association studies, are revealing new correlates of intelligence.

Why White Supremacists Are Chugging Milk (and Why Geneticists Are Alarmed)

Amy Harmon

White supremacists, who have long used science to justify their ideology, are misinterpreting new genetic research to justify racist conclusions, alarming some geneticists.

<u>'Could Somebody Please Debunk</u> This?': Writing About Science When Even the Scientists Are Nervous

Amy Harmon

Harmon reflects on the difficulty of writing her article on white supremacists' co-opting new genetic research for racist ends. She identifies as barriers 1) the lack of up-to-date information on genetics research for the general public, 2) scientists' reluctance to engage with the public and especially the far-right fringe, and 3) the proliferation of white supremacist, pseudo-scientific media on the internet.

Giant Study Links DNA to Same-Sex

Polygenic Risk Scores, School Achievement, and Risk for Schizophrenia: <u>A Danish Population-Based Study</u>

Holger J. Sørensen et al.

While poor academic performance in ninth grade strongly predicts later onset of schizophrenia, Sørensen and colleagues find that polygenic risk scores for schizophrenia do not predict poorer school performance and polygenic risk scores for educational attainment do not predict a diagnosis of schizophrenia.

The Genetics of University Success

Emily Smith-Woolley et al.

UK-based Twin analyses and genomewide polygenic scores analyzed by Smith Woolley and colleagues suggest a heritable element to enrollment and achievement in college education, as well as quality of college attended.

Education Can Reduce Health Differences Related to Genetic Risk of Obesity

Silvia H. Barcellos et al.

It has long been known that years of education and obesity are inversely related. New research shows that this is especially true for those with high polygenic risk scores for obesity, underscoring the role that changing social policies, like increasing the minimum age for legally dropping out of school, can have in mitigating genetically linked health differences.

<u>Genetic Consequences of Social</u> <u>Stratification in Great Britain</u>

Abdel Abdellaoui et al.

In a genome-wide association sample of 450,000 British residents, Abdellaoui et al. found 16 genetic traits that exhibited significant geographic clustering. Alleles associated with educational attainment (EA) showed the most clustering, with EAdecreasing alleles clustering in lower

Experiences

Michael Price

A new genome-wide association study identifies four chromosomal variations correlated with having same-sex sexual experiences. While the authors emphasize that the variations yield no predictive power, other researchers question the study's utility, arguing that it glosses over the difference between behavior and identity and makes room for stigmatization without providing benefits.

Life Span Has Little to Do with Genes, Analysis of Large Ancestry Database Shows

Sharon Begley

While previous estimates suggested that lifespan was 20 to 30 percent heritable, a new study of 54 million family trees finds that genes account for well under 7 percent of the human life span.

A New Test Can Predict IVF Embryos' Risk of Having a Low IQ

Clare Wilson

The firm Genomic Prediction is in talks with several IVF clinics to provide customers with newly developed genetic screening tests that can assess complex traits, such as low intelligence.

Offering Free DNA Sequencing, Nebula Genomics Opens for Business. But There's an Itsy-bitsy Catch

Sharon Begley

Nebula Genomics is offering consumers free genomic testing, provided they answer detailed demographic and health questions. Nebula will sell access to this data, socio-economic status areas such as coal mining areas.

<u>Making Sense of the Genome Remains a</u> <u>Work in Progress</u>

Wylie Burke

The uncertainties surrounding variants of unknown and only probable significance illustrate that care must be taken with the use and clinical communication of genetic testing results.

Reconceptualizing Harms and Benefits in the Genomic Age

Anya E.R. Prince and Benjamin E. Berkman

The lack of robust evidence of psychosocial harms and the expanding view that genomic research has indirect familial benefit should motivate advances in ELSI research on individual engagement with genetic and genomic information.

Epigenetic Aging in Major Depressive Disorder

Laura K.M. Han et al.

Compared with control subjects, patients with major depression exhibit higher epigenetic aging in blood and brain tissue, suggesting that they are biologically older than their corresponding chronological age; this effect is even more profound in the presence of childhood trauma.

Variation in TMEM106B in Chronic Traumatic Encephalopathy

Jonathan D. Cherry et al.

Post-mortem analysis of the brains of football players diagnosed with CTE reveals that a common gene variant (occurring in 43% of the population) associated with neuroinflammation in aging is protective against phosphorylated tau pathology, neuroinflammation, and ante-mortem dementia. along with the sequenced genome, to industry and academic researchers.

Many Families with Down syndrome Children Would Consider Gene Modification, but with Serious Concerns

Marsha Michie and Megan Allyse In this blog post follow-up to their June 2018 paper, Marsha Michie and Megan Allyse dive into the complicated feeling parents of people with Down syndrome have toward gene modification.

Why Is a Remote Colombian Town a Hot Spot of an Inherited Intellectual Disability?

Hannah Furfaro

A Colombian geneticist explores the genetic history of a small town with an unusually high prevalence of fragile X syndrome as part of his search to develop treatments.

<u>The Results of Your Genetic Test</u> <u>Are Reassuring. But That Can</u> <u>Change.</u>

Gina Kolata

Evolving analytical techniques mean that some genetic variants that were previously classified benign have been reclassified. Differences in companies' analyses can mean different results for the same genome, and no standard approach to communicating findings leaves individuals in the dark.

Massive Sequencing Project Identifies New Genetic Syndromes Jessica Wright

New research presented at the 2018 American Society of Human Genetics conference analyzed the

Using Genetics to Understand the Causal Influence of Higher BMI on Depression

Jessica Tyrrell et al.

Studying genetic variants shows that higher BMI, with and without its adverse metabolic consequences, likely has a causal, not just correlative, relationship with depression.

Nicotine Exposure of Male Mice Produces Behavioral Impairment in Multiple Generations of Descendants

Deirdre M. McCarthy et al.

Nicotine exposure in male mice produces epigenetic changes to sperm DNA and sex-dependent behavioral changes in subsequent generations, including deficits in learning and attention and increases in locomotor activity.

Spotlight on Pharmacogenetics

<u>The Use of Pharmacogenetic</u> <u>Testing in Patients with</u> <u>Schizophrenia or Bipolar Disorder: A</u> <u>Systematic Review</u>

Melanie Routhieaux et al.

Reviewing 18 studies, the authors find that tailoring antipsychotic medicine to patient genetics is not yet feasible in a clinical setting, especially given that none of the studies reviewed focused on clinical use of pharmacogenetics testing.

Pharmacogenetics in Psychiatry: A Companion, Rather Than Competitor, to Protocol-Based Care —Reply

Chad A. Bousman and Daniel J. Müller

Bousman and Müller argue that Zubenko and colleagues' September commentary, also in exomes of over 31,000 people with developmental delays and identified 302 associated genes. This will enable researchers, for example, to see which genes associated with autism show stronger ties to intellectual disability than to other features of autism.



Spotlight on *Current Opinion in Psychology*

Genetics, Volume 27

Eds. Brian Boutwell and Michael A. White

The June issue of Current Opinion in Psychology (still in progress) delves into the complex relationship between genetics and—among other topics—addiction, mental health, intelligence, autism, and antisocial behavior. Its review articles survey and assess existing literature, as well as probe topics like the hidden hypotheses in epigenome-wide association studies.

Spotlight on Secondary Findings

Responsibility, Identity, and Genomic Sequencing: A Comparison of published Recommendations and Patient Perspectives on Accepting or JAMA, incorrectly assumes that (1) all pharmacogenetic testing is created equal, and (2) pharmacogenetic testing is incompatible with protocol-based care. This leads to misplaced skepticism of the clinical utility of pharmacogenetics.

Pharmacogenetics in Psychiatry: A Companion, Rather Than Competitor, to Protocol-Based Care <u>—Reply</u>

George S. Zubenko et al. In response to criticism of their

September commentary, the authors argue that current pharmacogenetics studies lack rigor and that pharmacogenomics doesn't lead to clearly better outcomes; overall, the state of research doesn't suggest clinical utility at present, especially for major depressive disorder.

FDA Authorizes First Direct-to-Consumer Test for Detecting Genetic Variants That May Be Associated with Medication Metabolism

News Release

The FDA has authorized 23andMe to market a direct-to-consumer pharmacogenetics report. The panel, which detects 33 variants for multiple genes, is not intended to provide information on a patient's ability to respond to any specific medication. Furthermore, health care providers are not to use the test to make any treatment decisions.

<u>Companies Tout Psychiatric</u> <u>Pharmacogenomic Testing, But Is It</u> <u>Ready for a Store Near You?</u>

Declining Incidental Findings Felicity Boardman and Rachel Hale

Researchers interviewed 31 patients who were made aware of incidental findings from genetic testing. Participants' responses to incidental findings were tightly focused on one particular variant but also macroscopic—taking into account their personal biographies, social and biological relationships with known and unknown others, and broader sociopolitical contexts.

<u>The Preferences of Potential</u> <u>Stakeholders in Psychiatric Genomic</u> <u>Research Regarding Consent</u> <u>Procedures and Information Delivery</u>

Anna Sundby et al.

Sundby and colleagues find that stakeholders in psychiatric genomic research consider consent to be a reciprocal transaction between subjects and researchers, and that they value specific, dynamic, and inperson consent procedures.

Exploring Neurologists' Perspectives on the Return of Next Generation Sequencing Results to Their Patients: A Needed Step in the Development of Guidelines Hurlimann Thierry et al.

There is no consensus among neurologists regarding return of incidental findings or variants of unknown significance. However, Thierry and colleagues discover, there is more agreement on the perceived responsibility to recontact patients regarding newly discovered mutations related to the condition that triggered the test.

Secondary Findings from Clinical

Jennifer Abbasi

Albertson's and other major retailers will soon roll out pharmacogenetic testing and counselling through their pharmacies. But equivocal study results and clinicians' limited training in interpreting profiles suggest that such programs may have limited clinical benefit, while introducing new potential harms.

In the Race to Use Genetic Tests to Predict Whether Antidepressants Work, Science Might Be Getting Left Behind

Rebecca Robbins

There is a major push by academics, academic medical centers, and industry to make pharmacogenetics standard in psychiatric care, but, even more than in previous evolutions in the field, excitement outstrips evidence.

Genomic Sequencing: Prevalence, Patient Perspectives, Family History Assessment, and Health-Care Costs from a Multisite Study

M. Ragan Hart et al.

In a sample of 6240 participants who underwent genome or exome sequencing, 1.2% received secondary findings; disclosure of secondary findings showed little to no adverse impact on participants and added only modestly to nearterm health-care costs. In follow-up interviews with 18 patients, all patients indicated that they shared findings with relatives and that relatives did not pursue additional testing or care.

Upcoming Talks and Conferences

Moral Trajectories in Genomic Medicine:

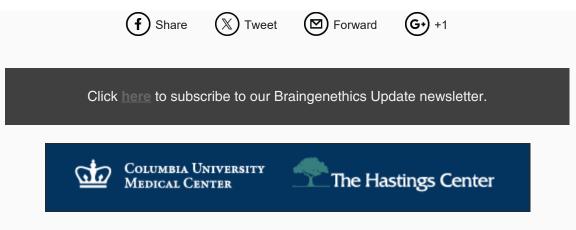
From Personalized Medicine to Precision Precision Prevention and Wellness

Genomics

Eric T. Juengst, PhD Director, UNC Center for Bioethics Professor, Departments of Social Medicine and Genetics University of North Carolina, Chapel Hill

Part of a seminar series on the ethical, legal and social implications of genetics Center for Research on Ethical/Legal/Social Implications of Psychiatric, Neurologic & Behavioral Genetics Department of Psychiatry, Columbia University Medical Center

Monday, December 17, 2018 12:00-1:00pm Rm. 10-204, Irving Institute for Clinical and Translational Research 10th Floor, Presbyterian Hospital (PH) Building, 622 W. 168th Street, NY



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