



PRESS RELEASE

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Genes that Help and Genes that Harm: Researchers Present New Findings on Genetic Factors Associated with Autism, Schizophrenia, and Parkinson's Disease

Genetics Experts to Present Cutting-edge Neuropsychiatric Research Developments at ICHG/ASHG 2011 Meeting on Genetic Causes of Autism, Schizophrenia, Intellectual Disability, Epilepsy, and a Gene that Protects Against Parkinson's Disease

BETHESDA, MD – September 29, 2011 – The world's top scientists and clinicians in the human genetics field will gather to present their latest research findings at the [12th International Congress of Human Genetics \(ICHG\) / 61st Annual Meeting of the American Society of Human Genetics \(ASHG\)](#), which will be held on October 11-15, 2011, at the Montreal Convention Center (Palais des Congrès) in Montreal, Quebec, Canada. A number of scientific presentations at the ICHG/ASHG 2011 Meeting will provide information about important new research developments that advance and expand our current understanding of genetic factors associated with autism spectrum disorder, schizophrenia, intellectual disability, epilepsy, and other neuropsychiatric conditions.

ASHG will be hosting a press briefing session (which will also be made available to the media as an online webcast) to highlight four presentations of interest on this topic at the ICHG/ASHG 2011 Meeting. The abstracts presented in this press briefing will address exciting new research findings that shed light on the underlying genetic factors that cause (or increase a person's risk of developing) neuropsychiatric conditions, including autism spectrum disorder, intellectual disability, and epilepsy. In addition, one of the abstracts presented in this press briefing will highlight the results of a new gene-environment interaction study that has identified a modifier gene that reduces the risk of developing Parkinson's disease when combined with coffee consumption (i.e., in individuals who drink coffee regularly). The final abstract presented in this press briefing will describe the results of a study that identified genes responsible for schizophrenia in consanguineous (intermarried) Palestinian families with multiple affected cases.

Members of the media are invited to attend this press briefing session entitled, "*Genes that Help and Genes that Harm: New Findings on Genetic Factors Associated with Autism, Schizophrenia, and Parkinson's Disease*," which will be held on Friday, October 14, 2011, from 2:30-3:30 p.m. in the ICHG/ASHG Press Briefing Room, located in Room 518A on the fifth floor of the Montreal Convention Center. **[To view the online webcast recording of this press briefing event, please go to: http://www.ashg.org/ichg2011/NeuropsychGenetics](http://www.ashg.org/ichg2011/NeuropsychGenetics)** (*see section below for more information about this webcast).

After a brief introduction by session moderator [Evan Eichler, PhD](#), each of the following four press briefing speakers will discuss their research abstracts presented at the ICHG/ASHG 2011 Meeting on important new findings that advance and expand our understanding of the genetics of autism spectrum disorder, Parkinson's disease, schizophrenia, and other neuropsychiatric conditions:

- **Evan Eichler, PhD** (*Moderator*) – [“Copy Number Variation and Variability in Autism and Neuropsychiatric Disease”](#)
- **Cynthia Morton, PhD** – [“Assessment of Chromosome 2q23.1 Microdeletion Syndrome Implicates MBD5 Gene as a Single Causal Locus of Autism Spectrum Disorders, Intellectual Disability, and Epilepsy”](#)

- **Haydeh Payami, PhD** – [“Genome-Wide Gene-Environment Study Identifies Glutamate Receptor Gene *GRIN2A* as a Parkinson’s Disease Modifier Gene via Interaction with Coffee”](#)
- **Hashem Shahin, PhD** – [“Gene Discovery for Schizophrenia by Exome Sequencing of Multiply-affected Consanguineous Palestinian Families”](#)

Brief summaries of the content covered in these four presentations are included in the section below:

[Copy Number Variation and Variability in Autism and Neuropsychiatric Disease*](#)

[Evan E. Eichler, PhD](#) (Session Moderator), *Principal Investigator and Professor, Department of Genome Sciences, University of Washington, Seattle; Howard Hughes Medical Institute (HHMI) Investigator*

Autism and intellectual disability are both neurodevelopmental disorders comprised of patients representing a constellation of numerous conditions that manifest themselves at varying degrees of severity. Both of these types of neuropsychiatric disorders have a genetic component, yet the genetic factors that cause autism are only known for fewer than 20% of cases, and more than 90% of patients have no known family history of the disease. The study of potential genetic factors that play a role in the development of autism spectrum disorders is complicated by the fact that so many cases are sporadic (only one case present in the family).

Several presenters will give an overview of their major research findings on the genetics of autism and intellectual disability in an Invited Scientific Session at the ICHG/ASHG 2011 Meeting on [“Intellectual Disability and Autism: Two Sides of the Same Coin.”](#) One of the speakers in this session, [Evan Eichler, PhD](#), a Principal Investigator and Professor in the Department of Genome Sciences at the University of Washington, Seattle, will present his research on [copy number variation and variability in autism and complex neuropsychiatric disease](#).

In this press briefing, Dr. Eichler will discuss the results of a recent research study he conducted that analyzed the genomes of children with developmental delay compared to healthy adult controls. The results of his analysis suggest that as much as 14% of pediatric disease, including autism, epilepsy, and heart defects, is caused by deletions and duplications of large segments of the genome involving multiple genes. These structural rearrangements of large sections of the genome – which are also known as copy number variants (or CNVs) – result in an abnormal number of copies of genes or intergenic regions. These mutations can either be inherited or caused by spontaneous disruptive mutations, which are also known as [de novo mutations](#). Eichler will discuss his findings that indicate some of same disease-causing mutations can manifest very differently in different individuals, and in particular, be more severe if they occur along with other compounding mutations.

Based on his analyses, Eichler expects that the overall burden of rare and unique severe mutations will help predict different outcomes ranging from autism, intellectual disability, and epilepsy. Eichler proposes that the early development of the brain is particularly sensitive to the timing and expression of many different genes, and that multiple genetic perturbations within specific pathways can lead to autism and other types of neuropsychiatric diseases with varying degrees of severity.

*[*Presented in ICHG 2011 Invited Scientific Session: [“Intellectual Disability and Autism: Two Sides of the Same Coin”](#)]*

[Assessment of Chromosome 2q23.1 Microdeletion Syndrome Implicates *MBD5* Gene as a Single Causal Locus of Autism Spectrum Disorders, Intellectual Disability, and Epilepsy](#)

[Cynthia C. Morton, PhD](#), *Editor of The American Journal of Human Genetics (ASHG’s scientific journal); Director of Cytogenetics, Brigham and Women’s Hospital; William Lambert Richardson Professor of Obstetrics, Gynecology and Reproductive Biology and Professor of Pathology, Harvard Medical School*

Although persons with neurodevelopmental disorders or autism spectrum disorder (ASD) often harbor deletions of large chromosomal regions and display similar clinical characteristics, which are referred to as microdeletion syndromes, the individual genetic factors that contribute to such abnormalities within these regions have been very difficult to pinpoint.

A group of researchers led by [Cynthia C. Morton, PhD](#), who currently serves as Editor of ASHG’s scientific journal, [The American Journal of Human Genetics \(AJHG\)](#), and as Director of Cytogenetics at Brigham and Women’s Hospital, and Professor of Obstetrics, Gynecology and Reproductive Biology at Harvard Medical

School, established a consortium to accumulate and analyze data from a large cohort of subjects with genetic alterations of chromosome 2q23.1 (in collaboration with Sarah Elsea, PhD, Michael Talkowski, PhD, and James Gusella, PhD). The group's study results are being presented in a [platform session at the ICHG/ASHG 2011 Meeting](#), and the findings are also being published in the October 2011 issue of *The American Journal of Human Genetics* in a paper entitled, "Assessment of 2q23.1 Microdeletion Syndrome Implicates MBD5 as a Single Causal Locus of Autism Spectrum Disorder, Intellectual Disability, and Epilepsy."

The authors assembled an open collaboration to find patients with chromosomal rearrangements involving chromosome 2q23.1 that might point to an important gene for neurodevelopmental disorders. The consortium identified 65 individuals with alterations of chromosome 2q23.1, including two translocations that disrupted the region. The authors found that only a single gene, called methyl-CpG binding domain 5 (*MBD5*), was disrupted by all 65 variations, suggesting this gene represents a critical region that when deleted can lead to developmental abnormalities. They also found consistent deficiencies in expression of the gene, regardless of the size or region of the genetic alteration. *MBD5* is known to be an important protein in the epigenetic regulation of gene expression.

The large size of the cohort analyzed in their study enabled identification of a core set of features common to all individuals with disruption of *MBD5*, which include intellectual disability, developmental delays, epilepsy, language impairment, and behavioral problems, as well as ASD. The research team also identified a variation in the critical methyl-binding domain of *MBD5* that could confer genetic risk for ASD, although more studies are needed to determine the exact impact of this variant. Overall, the results of their analyses suggest that microdeletions of *MBD5* occur at a frequency of approximately 1/500–1/1000 ASD cases, and the mutation was present in ~0.8% of ASD cases compared to 0.07% of controls.

Taken together, these results confirm that the *MBD5* gene is a primary contributor to the developmental abnormalities observed in 2q23.1 chromosome microdeletion syndrome, and alterations of the gene could represent a significant genetic risk factor for ASD. Furthermore, because *MBD5* alone is associated with a distinct syndromic disorder, it is worthy of consideration in the diagnostic evaluation of individuals with ASD, particularly in cases that are complicated by epilepsy and intellectual disability.

[Genome-Wide Gene-Environment Interaction Study Identifies *GRIN2A* as a Modifier Gene that Reduces Parkinson's Disease Risk via Interaction with Coffee](#)

[Haydeh Payami, PhD](#), Professor of Genetics and Neurology, New York State Dept. of Health Wadsworth Center

Genes and environment both play important roles in the development of most health conditions, including psychiatric disorders such as Parkinson's disease, which is a progressive, age-related movement disorder that is the second most common adult-onset neurodegenerative disorder worldwide, affecting 1-2% of people over the age of 65. Parkinson's disease, like most common disorders, involves interactions between genetic make-up and environmental exposures, which are unique to each individual. Previous studies have found an inverse association between caffeinated coffee consumption (an environmental factor) and the risk of developing Parkinson's disease. However, not everyone benefits equally from getting their caffeine fix on a regular basis since the protective effects of drinking coffee are also dependent on a person's genes.

The NeuroGenetics Research Consortium (NGRC), an international team of researchers led by [Haydeh Payami, PhD](#), a Professor of Genetics and Neurology at the New York State Department of Health Wadsworth Center, conducted a study to further investigate the genetic factors that contribute to this relationship by identifying genes that influence the inverse association of coffee with the risk of developing Parkinson's disease. Payami's experiment was a genome-wide association study (GWAS), but with a new twist – coffee consumption was added as a variable so the interaction between genes and coffee could be tested. The study was conducted using the NGRC data set which included 2,500 research volunteers, each of whom was genotyped for about one million genetic markers and had lifetime caffeinated coffee consumption data. The researchers performed a genome-wide association and interaction study (GWAIS) to analyze genome sequence data and compare it against caffeinated coffee consumption data for 1,458 persons with Parkinson's disease and 931 healthy individuals from the NGRC data set.

Their analysis revealed a stronger association with the *GRIN2A* gene and caffeine consumption than with previously recognized genetic risk factors in Parkinson's disease. The *GRIN2A* gene plays an important role in the functioning of the central nervous system, since it codes for a unit of a molecule involved in excitatory

neurotransmission and control of movement and behavior. The current research findings indicate that the *GRIN2A* signal was present in significant amounts in the heavy coffee drinkers, but not in the light coffee drinkers. Overall, heavy coffee consumption was associated with 27% risk reduction on average; however, when divided by *GRIN2A* genotype, one group had 18% risk reduction and the other 49%.

The study is important for three reasons. First, the results may lead to personalized prevention and treatment for Parkinson's disease. Glutamate-antagonists (*GRIN2A*-related) are currently being tested in clinical trials for treatment of Parkinson's disease; *GRIN2A* may therefore be a useful pharmacogenetic marker for prevention and treatment trials and therapy, which warrants further investigation. Second, it demonstrates that it is possible to study gene-environment interactions on a large genome-wide scale, and this approach can identify important genes that are missed when environmental exposures are not taken into account. Third, discovery of the interaction between *GRIN2A* (which is involved in neurotransmission in the brain) and caffeine (which is an adenosine-A_{2A}-receptor antagonist) may help elucidate the cause and progression of Parkinson's disease.

Genomic Analysis of Schizophrenia in Consanguineous Palestinian Families with Multiple Affected Cases Identifies New Genetic Mutations Associated with the Disease

Hashem Shahin, PhD, Assistant Professor of Biology, Department of Life Sciences and Hereditary Research Laboratory, Bethlehem University, Bethlehem, Palestine

Schizophrenia, a debilitating mental disorder, affects nearly one percent of the population. Family, twin, and adoption studies all support a strong genetic component for schizophrenia, but the genetic causes of schizophrenia remain elusive. Scientists have long been interested in studying the possible association between consanguinity and neurodevelopmental to get a better understanding of the genetic causes of schizophrenia.

A team of researchers led by Principal Investigator Hashem Shahin, PhD, an Assistant Professor of Biology in the Department of Life Sciences and Hereditary Research Laboratory at Bethlehem University in Palestine (in collaboration with Professors Mary-Claire King and Tom Walsh from the University of Washington, Seattle), conducted a study to identify genes responsible for schizophrenia in consanguineous Palestinian families. Traditional marriage patterns among close and extended family members have produced high rates of consanguinity among these groups. Marriage between first cousins is seen in more than one third of the families in these populations, and it is estimated that marriage among members of extended families may comprise up to 60% of all marriages. As a result, recessively inherited phenotypes, whether purely Mendelian or complex, are common among families in this population. These families present an ideal opportunity to study the possibility that rare mutations that are expressed as a recessive abnormality in neurodevelopment or schizophrenia.

Shahin and his colleagues studied affected and unaffected family members from families in this population that exhibited a high incidence of severe schizophrenia. For all affected individuals, the researchers sequenced regions of the genome that are known to be 'hotspots' for copy number variations (CNVs) associated with schizophrenia in order to rule these out as genetic factors contributing to the disease. Once these regions were ruled out, Shahin's team identified unique or rare single nucleotide polymorphisms (SNPs) and insertion/deletion variants in affected individuals by comparing them to common variants in the population. The frequency of these unique variants was then compared among affected versus unaffected individuals within consanguineous families, and determined for the population as a whole. The resulting variants that are truly unique to individuals affected by schizophrenia have led to the identification of compelling candidate mutations for schizophrenia, some of which are found in genes that have previously been implicated in idiopathic mental retardation.

PRESS BRIEFING SESSION & WEBCAST INFORMATION

ASHG invites members of the media to attend this press briefing on the latest developments in neuropsychiatric disease genetics research, which will be held Friday, October 14, 2011, from 2:30-3:30 p.m. in the ICHG/ASHG Press Briefing Room (located in Room 518A on the fifth floor of the Montreal Convention Center). To register onsite as a member of the media, you must bring your press credentials* with you to the ICHG/ASHG Press Office in Room 518B (Level 5) upon arrival at the Montreal Convention Center in order to obtain a press badge.

Please note that the online webcast recordings of ASHG's press briefing events at the ICHG/ASHG 2011 Meeting will not be webcast live. **To view the online webcast recording of this press briefing, click on the**

link below about an hour after the event has ended (the webcast will be posted on ASHG's Web site at the following URL by 4:30 p.m. on Friday, Oct. 14, 2011): <http://www.ashg.org/ichg2011/neuropsychgenetics/>.

About The American Society of Human Genetics

Founded in 1948, the [American Society of Human Genetics \(ASHG\)](http://www.ashg.org) is the primary professional membership organization for human genetics specialists worldwide. The nearly 8,000 members of ASHG include researchers, academicians, clinicians, laboratory practice professionals, genetic counselors, nurses and others with a special interest in human genetics. The Society's mission is to serve research scientists, health professionals and the public by providing forums to: (1) share research results through the [ASHG Annual Meeting](#) and in [The American Journal of Human Genetics \(AJHG\)](#); (2) advance genetic research by advocating for research support; (3) educate current and future genetics professionals, health care providers, advocates, policymakers, educators, students, and the public about all aspects of human genetics; and (4) promote genetic services and support responsible social and scientific policies. For more information about ASHG, please visit our Web site at: <http://www.ashg.org>.

About The International Congress of Human Genetics

The [12th International Congress of Human Genetics \(ICHG\)](http://www.ichg2011.org), which is sponsored by the American Society of Human Genetics (ASHG) in partnership with the International Federation of Human Genetics Societies (IFHGS), is the foremost meeting of the worldwide human genetics community, and it is held every five years. In 2011, the 12th ICHG Meeting will be the major focal point and platform for the world's most exciting research, and attendance at this year's meeting is anticipated to be more than 7,000 delegates from over 60 countries around the world. For more information about the ICHG Meeting, go to: <http://www.ichg2011.org>.

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**Please note that all press registrants will be required to provide appropriate media credentials and identification to ASHG Press Office staff before receiving a press badge to access meeting events.*

<p>ASHG EXPERTS & PRESS BRIEFING SPEAKERS AVAILABLE FOR INTERVIEW</p>
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