

## NEWS

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### **Genomas Announces Physiogenomic Study That Reveals Potential Cause of Metabolic Side Effects in Patients Treated with Psychotropic Drugs**

*-- Research published in Molecular Psychiatry heralds DNA-guided, safer patient treatment with psychotropics--*

**HARTFORD, Conn., January 4, 2007** – Genomas, Inc. today announced the publication of a foundational paper that describes potential DNA markers for risk and protective factors involved in diabetes-related metabolic side effects from treatment with common antipsychotic drugs. The research, which was published in the January 2, 2007 online issue of Nature Publishing Group's *Molecular Psychiatry*, highlights how understanding a patient's DNA can predict an individual's profile of risk or protection from the antipsychotic drugs prescribed, and thus provide clinicians with better options for drug selection or further preventative treatment. The study, entitled "Physiogenomic comparison of weight profiles of olanzapine- and risperidone-treated patients", looked at two of the leading atypical antipsychotic medicines on the market and found that a series of unique DNA variations could predict a patient's likelihood for developing pre-diabetic side effects such as weight gain.

The use of antipsychotic drugs is on the rise, with an estimated 14 million patients suffering from chronic mental health disorders -- such as schizophrenia, bipolar disorder, obsessive-compulsive disorder, and generalized anxiety disorder -- for which these drugs are increasingly being prescribed. Atypical antipsychotics (AAPs) can induce diabetic symptoms in nearly one third of patients, most notably characterized by increased weight gain in some patients but not in others. However, the side effect profiles for these drugs even within the same drug class may differ, raising the possibility of drug-specific side effects.

“From a clinical standpoint, these drugs are an important part of the physician’s armamentarium, and the ability to select the appropriate one for each patient to gain therapeutic impact without metabolic side effects would be a major advance,” noted Dr. Jose de Leon, co-author of the paper, and Professor of Psychiatry, College of Medicine, University of Kentucky, and Medical Director, University of Kentucky Mental Health Research Center at Eastern State Hospital. “This approach is precisely how we envision the process of personalized medicine affecting the practice of psychiatry.”

“Pharmacogenomic screening has rapidly become the most promising tool on psychiatry’s therapeutic horizon,” said Harold I. Schwartz, M.D., Psychiatrist-in-Chief and Vice President, Behavioral Health, Institute of Living/Hartford Hospital. “The capacity to tailor the choice of psychotropic medication to reduce the risk of metabolic syndrome and other debilitating side effects will spare our patients untold suffering. This type of research is leading the way to the future of psychiatric therapeutics.”

The studies were undertaken using Genomas’ PhysioGenomics Technology, a proprietary biomedical platform that analyzes DNA variation within a patient population and compares these differences to physiological characteristics or reactions. PhysioGenomics Technology looks at the entire distribution of patients’ responses and determines how the frequency of single nucleotide polymorphisms (SNPs) varies among individuals with similar responses to a drug. When configured into SNP ensembles with interpretative algorithms, the company’s product, termed “Phyziotype” system, enables clinicians to perform DNA-guided drug selection considering an individual’s innate likelihood of developing side effects.

## **STUDY OVERVIEW AND FINDINGS**

The *Molecular Psychiatry* study followed patients who were part of ongoing genotyping studies at the Institute of Living, Hartford, Connecticut and at three Kentucky state hospitals: 67 patients taking olanzapine and 101 taking risperidone were sampled for genotyping. A total of 29 SNPs were selected from 13 candidate genes related to peripheral lipid homeostasis or central appetite regulation, key indicators of pre-diabetic conditions.

The investigators assessed the physiological-genomic associations with the weight profiles of patients in either drug. Age, gender, race, and site (Kentucky or Connecticut) were also analyzed as potential covariates. The data show that physiogenomic associations of patient weight profiles can be established for genes in the pathways encompassing appetite peptides and peripheral lipid homeostasis, thereby differentiating olanzapine and risperidone side-effect profiles. Specifically, the researchers found that a certain series of SNPs in cholesterol metabolism-related genes coding for apolipoproteins E and A4 were significantly associated with the weight profile in the olanzapine-treated group but

not in the resperidone group. Conversely, it was found that a different series of SNPs in appetite-related genes coding for leptin receptor and neuropeptide Y receptor Y5, were significantly associated with the weight profile of the resperidone-treated group but not in the olanzapine counterpart. Gender was also found to be significantly associated in the resperidone-treated group, with men being heavier on average.

“AAPs are a very effective and useful drug class. However, they have a detrimental metabolic impact on certain patients in which they induce pre-diabetic symptoms,” noted Dr. Gualberto Rúaño, President of Genomas. “Our goal at Genomas is to provide physicians with DNA-guided decision support to prescribe the safest drug to each patient. In follow up to this research, we plan clinical validation studies for these drugs and DNA markers and extension of our physiogenomic discovery to other psychotropic drugs on the market.”

The research was conducted by scientists at several leading institutions, including G. Rúaño, M. Kocherla, and A. Windemuth of Genomas Inc.; J.W. Goethe, C. Caley, and S. Wooley of the Institute of Living, Hartford Hospital; T.R. Holford of Yale University School of Medicine; and J. de Leon, Department of Psychiatry, College of Medicine, University of Kentucky, and University of Kentucky Mental Health Research Center at Eastern State Hospital.

#### **ABOUT GENOMAS**

Genomas®, Inc. is a biomedical company advancing DNA-guided medicine and personalized health. The company develops revolutionary PhyzioType™ systems for DNA-guided diagnosis and treatment of metabolic disorders induced by drugs and by diabetes in cardiovascular and psychiatric medicine. PhyzioType™ systems provide physicians with the unprecedented capability to select for each patient the safest drug treatment and the most effective disease prevention. Genomas is located in Hartford, CT on the campus of Hartford Hospital. For more information please access [www.genomas.net](http://www.genomas.net)

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