

### **Jose de Leon's Narrative Report (September 6, 2015)**

Academic career: Dr. Jose de Leon is a native of Bilbao, Spain, and received his medical training at the University of Navarre in Spain. He came to the United States in 1987 to hone his research skills in psychiatry. He completed fellowships in clinical psychopharmacology in Philadelphia. He was named Research Assistant Professor in the Department of Psychiatry at the Medical College of Pennsylvania and Hahnemann University in 1991. In 1995 he was promoted to Research Associate Professor. In 1996 he moved with his family to Lexington, Kentucky, where he became Associate Professor at the University of Kentucky (UK) Department of Psychiatry. In 2006 he was promoted to Professor in the Colleges of Medicine and Pharmacy. He has served as Medical Director for the Mental Health Research Center at Eastern State Hospital (ESH) since 1996.

Clinical activities: Dr. de Leon served as ESH staff physician for the treatment-refractory unit for 8 years. He has been serving as a consultant for the Kentucky Department for Mental Health, Developmental Disabilities and Addiction Services since 2001. In that role, he assists clinicians caring for patients with complex psychiatric illnesses at mental health and intellectual disability public facilities by sharing his psychiatric and medical expertise. He investigates deaths at the mental health public system, and develops and publishes specialized pharmacological guidelines for intellectual disability facilities.

Educational activities: Dr. de Leon's ongoing work with UK psychiatric residents and pharmacists at ESH has resulted in several articles and special recognition awards from the residents. He developed a set of PowerPoint presentations to teach pharmacodynamics and pharmacokinetics of psychiatric drugs using many real psychiatric patient cases that will be placed at INHN. Many of these cases have already been published in peer-reviewed journals. He has collaborated with several research groups in Spain and facilitated the career development of Spanish researchers who are internationally known in the areas of schizophrenia, bipolar disorder and suicide. Since 1998, Dr. de Leon has been a Visiting Professor at the Federico Oloriz Neuroscience Institute, Medical School, University of Granada, Granada, Spain. From 2003 to 2009, he was a "Voluntary Professor" at the Department of Statistics, Science School, Universidad Nacional, Medellin, Colombia.

Research activities: Dr. de Leon's research career has been prolific. He is an expert in schizophrenia, psychopharmacology, pharmacogenetics and personalized medicine. He has received grants from the NIH, NARSAD and industry. His most ambitious study was described in *Business Week's* September 5, 2005, cover article entitled "Drugs Get Smart" and was also published in *CNS Spectrums* in 2009 (14:19-34). Over 4500 participants from three Kentucky state hospitals were recruited for this study; their CYP2D6 and CYP2C19 genetic profiles were studied using the first DNA microarray approved for clinical use by the FDA (the AmpliChip CYP 450 Test). He has published 275 peer-reviewed manuscripts described in PubMed, including one in *Science* (a letter), 30 in the *Journal of Clinical Psychiatry*, 24 in the *Journal of Clinical Psychopharmacology* and 22 in *Schizophrenia Research*. Many preprinted articles are available at [http://uknowledge.uky.edu/do/search/?q=author\\_lname%3A%22de%20Leon%22%20AND%20author\\_fname%3A%22Jose%22&start=0&context=1674591&sort=date\\_desc](http://uknowledge.uky.edu/do/search/?q=author_lname%3A%22de%20Leon%22%20AND%20author_fname%3A%22Jose%22&start=0&context=1674591&sort=date_desc)

The Science Citation Index and the Social Science Citation Index developed by the Institute of Scientific Information (ISI) reflect the number of times articles are cited, and are used to calculate the impact factor of articles. A June 2015 ISI Web of Science computer search showed that Dr. de Leon's scientific publications have been cited in the literature more than 6000 times. Hirsch (*PNAS* 102:16569-72, 2005) proposed the "h" index to summarize a researcher's articles. Dr. de Leon's "h" index is 43 (he has at least 43 articles with at least 43 citations each).

His most important scientific contributions to the literature include demonstrating 1) the association of polydipsia with smoking and schizophrenia in patients with severe mental illness; 2) that the association between smoking and schizophrenia is present worldwide, and may be partly explained by

shared vulnerability; 3) the direct effects of olanzapine (not explained by weight) and other antipsychotics on triglyceride levels using complex statistical techniques to control for the effects of weight gain; 4) that CYP3A4 inducers and CYP2D6 poor metabolizer phenotype may influence risperidone pharmacokinetics and response; and 5) valproate's inductive properties for olanzapine and clozapine metabolism.

For the last 15 years, Dr. de Leon has focused on developing concepts and practical methods for implementing personalized medicine in psychiatry. To accomplish this, he collaborates with Francisco J. Diaz, Ph.D., a statistician at the University of Kansas; Edoardo Spina, M.D., Ph.D., a clinical pharmacologist at the University of Messina, Italy; and Chin Eap, Ph.D., a pharmacologist at the Universities of Geneva and Lausanne, Switzerland. Dr. de Leon views personalized prescription as the branch of personalized medicine focused on individualizing pharmacological treatments that can be implemented as personalized drug dosing and personalized drug selection by considering genetic, environmental and personal factors. With his collaborators, Dr. de Leon is focused on antipsychotic therapeutic drug monitoring, using random-effects linear models (or linear mixed models) to study antipsychotic levels, and developing correction factors that allow personalized antipsychotic dosing according to genetic, environmental and personal factors.

Since 2013, he has been writing a set of articles on the future of psychiatry and the recent publication of the *DSM-5*, taking into account the traditional concepts of descriptive psychopathology put forth by Karl Jaspers one century ago in his textbook *General Psychopathology*.