

Jose de Leon's Narrative Report (September 10, 2018)

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 for 4 years. In 1991, he was named Research Assistant Professor in the Department of Psychiatry at the Medical College of Pennsylvania and Hahnemann University and, in 1995, 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. Since 2001, he has been serving as a consultant for the Kentucky Department for Mental Health, Developmental Disabilities and Addiction Services. 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 within the public mental health system, and develops and publishes specialized pharmacological guidelines for medical providers working in facilities for the intellectually disabled (40 drug guidelines, of which 28 have been published).

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 titled "Training Psychiatrists to Think Like Pharmacologists" to teach the pharmacodynamics and pharmacokinetics of psychiatric drugs using many real psychiatric patient cases. The course is available at <http://inhn.org/home/courses/jose-de-leon-training-psychiatrists-to-think-like-pharmacologists.html>, a web page developed by INHN (International Network for the History of Neuropsychopharmacology). The 2015-6 psychopharmacology course has 12 theoretical lectures and 18 cases. Most of these cases have already been published in peer-reviewed journals. Dr. de Leon has mentored research groups around the world. In particular, he has facilitated the career development of Spanish researchers who are internationally known in the areas of schizophrenia (Victor Peralta, M.D, with an h-index of 43 at ResearchGate in September of 2018), bipolar disorder (Ana Gonzalez-Pinto, M.D, with an h-index of 44 at ResearchGate in September of 2018) and suicide (Enrique Baca-Garcia, M.D, with an h-index of 38 at ResearchGate in September of 2018). 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 more than 300 peer-reviewed manuscripts described in PubMed. Most of them are in psychiatric journals (63%), pharmacological journals (7%) or journals considered to be both psychiatric and pharmacological journals (20%). Other articles were published in genetic, medical, psychological or epidemiological journals and one was published in *Science* (a letter). Many preprinted articles are available at http://uknowledge.uky.edu/do/search/?q=author_iname%3A%22de%20Leon%22%20AND%20author_fname%3A%22Jose%22&start=0&context=1674591&sort=date_desc or ResearchGate https://www.researchgate.net/profile/Jose_De_Leon

ResearchGate (<https://www.researchgate.net>) offers information similar to the better-established Institute of Scientific Information (ISI), which calculates the impact factor of articles. ResearchGate includes more articles than ISI and can be freely accessed after registration. Hirsch (PNAS 102:16569-72, 2005) proposed the “h” index to summarize a researcher’s articles. According to ResearchGate in September 2019, Dr. de Leon’s scientific publications have been cited more than 12,000 times, and had more than 30,000 reads. He has an h-index of 59 (he has at least 59 articles with ≥ 59 citations).

His most important scientific contributions to the literature include demonstrating 1) that the association between smoking and schizophrenia is present worldwide, and may be partly explained by shared vulnerability; 2) the association of polydipsia with smoking and schizophrenia in patients with severe mental illness; 3) that CYP3A4 inducers and the CYP2D6 poor metabolizer phenotype may influence risperidone pharmacokinetics and response; 4) valproate’s inductive properties for olanzapine and clozapine metabolism, and 5) that a small number of psychiatric patients behave as ultrarapid metabolizers due to genetic or drug-drug interactions and need high doses of atomoxetine, risperidone, clozapine, valproate or lamotrigine, or have unusual responses due to activation of hydrocodone, oxycodone or diphenhydramine.

Since he came to Kentucky 22 years ago, Dr. de Leon has concentrated on using therapeutic drug monitoring and pharmacogenetics for implementing personalized medicine in psychiatry and studying drug-drug interactions. 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; Chin Eap, Ph.D., a pharmacologist at the Universities of Geneva and Lausanne, Switzerland; and Christoph Hiemke, Ph.D., the leader of the Arbeitsgemeinschaft für Neuropsychopharmakologie und Pharmakopsychiatrie (AGNP) and the developer of consensus guidelines for therapeutic drug monitoring in psychiatry. 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/or personalized drug selection based upon consideration of 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. In 2015 he started collaborating with a group of Chinese collaborators at the Beijing Anding Hospital.

Since 2013, he has been writing a set of articles on the future of psychiatry and the 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*. Dr. de Leon believes that US psychiatry is currently dominated by an extreme form of biological reductionism.