

The U.S./Costa Rica Neuropsychiatric Genetics Research Training Program

Providing advanced training opportunities to Costa Rican neuropsychiatric researchers

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The U.S./Costa Rica Neuropsychiatric Genetics Research Training Program (USCRNGRTP) represents a 10-year collaborative effort between universities in Texas and Costa Rica to provide research training experiences for clinicians and scientists from Costa Rica in the areas of psychiatric and neuropsychiatric genetic research. This effort finds its roots more than 20 years ago, when researchers from the University of Costa Rica, led by Dr. Pedro Leon, began to perform research in collaboration with investigators from the United States, to identify a gene causing inherited deafness (Leon, Raventós, Lynch, Morrow, & King, 1992). In the early 1990s, these research studies expanded to include a study on the genetics of bipolar disorder (Escamilla, Spesny, Reus, Gallegos, Meza, Molina, Sandkuijl, Fournier, Leon, Smith, & Freimer, 1996). The promise of conducting research studies for complex illnesses with a strong genetic basis was further stimulated by research by Dr. Escamilla and colleagues which suggested that the Central Valley of Costa Rica could serve as a model location for studying the genetics of human psychiatric disease (Escamilla et al., 1996).

Within the next decade, a number of additional studies followed in the genetics of schizophrenia, Tourette's disorder, autism and asthma (Hare, Glahn, Dassori, Raventos, Nicolini, Ontiveros, Medina, Mendoza, Jerez, Muñoz, Almasny, & Escamilla, 2010; Mathews, Waller, Glidden, Lowe, Herrera, Budman, Erenberg, Naarden, Bruun, Freimer, & Reus, 2004; McInnes, González, Manghi, Esquivel, Monge, Delgado, Four-

nier, Bondy, & Castelle, 2005; Celedón, Soto-Quiros, Avila, Lake, Liang, Fournier, Spesny, Hersh, Sylvia, Hudson, Verner, Klanderma, Freimer, Silverman, & Weiss, 2007). An important task in conducting this research work was to build collaborative teams between Costa Rican clinicians and scientists and colleagues from universities in the United States and elsewhere. Education and teaching of Costa Rican scientists and clinicians initially took place within the context of specific research studies, beginning in the late 1980s with a sabbatical completed with Dr. Leon at the University of California in Berkeley, and continued as the projects in bipolar disorder and schizophrenia progressed in the 1990s.

By the early 2000s, research projects funded by the National Institute of Mental Health in the United States included at least five active grants (Molecular and Population Genetics of Bipolar Disorder, K02MH001375; Genetic and Epidemiologic Studies of Bipolar Disorder, R01MH049499; Genotypic and Phenotypic Studies of Bipolar Disorder, K01MH001453; Genetics of Schizophrenia in Latino Populations, R01MH060881; Population Based Mapping of Schizophrenia Genes, R01MH061884). As these grants proceeded, a collaborative network of investigators in both countries developed which has continued to this day. This informal network of senior scientists runs the gamut of fields reflecting today's multidisciplinary research environment, including molecular biologists, psychiatric clinicians and statistical geneticists. In 2002, the first formal research training program was born, supported

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by the mentorship, leadership and resources of this international network, and embedded within ongoing research projects between investigators in San Antonio, Texas and the University of Costa Rica in San José.

This first incarnation of the research training program for Costa Rican scientists was named the U.S./Costa Rica Psychiatric Genetics Research Training Program, reflecting a specific focus on psychiatric illness (this is in contrast to the current program model, which expanded to focus more broadly on neuropsychiatric illness). This program was sponsored by a 5-year grant (D43TW006152) from the Fogarty International Center of the U.S. National Institutes of Health, a government agency which serves as one of the premier funding sources for biomedical research in the U.S. and internationally. Applied for in March, 2002 and awarded in September of the same year, the psychiatric research training program (RTP) was a response to a solicitation posted by the Fogarty International Center seeking programs designed to support scientists from low- to middle-income countries to receive research training in areas related to chronic, non-communicable diseases (NCDs).

In many ways, Costa Rica was an ideal location for developing this specific type of program. For one, psychiatric (and neuropsychiatric) illnesses belong to the class of chronic, non-communicable diseases. Furthermore, not only are psychiatric and neuropsychiatric illnesses NCDs, they have also been shown to constitute one of the leading disease burdens throughout the world, according to World Health Organization data (WHO, Global Burden of Disease, 2004). Given the severity and extent of the problem presented by psychiatric and neuropsychiatric illness, it is to be expected that a commensurate number of researchers would exist devoted to helping to solve this public health issue. Results from the literature, however, have shown that this is frequently not the case. According to one report, Costa Rica represents a particular case where the country has been shown to be lagging in its scientific development, finding there to be 1.03 researchers per 1,000 economically active persons in Costa Rica, relative to 13.75 in the U.S., 6.36 in Spain, and 2.57 in Argentina, also ranking behind the Iberoamerican

regional average found in the study, 1.33 (MICIT-CO-NICIT, 2001). In the midst of a lack in overall scientific development in Costa Rica, the research training team also made the striking observation that as late as 2002 “no Costa Rican psychiatrists had completed extensive research training (postdoctoral research fellowships),” and that “there was limited experience and faculty trained in understanding how to conduct research in complex genetic disorders and chronic diseases” (NIH proposal, D43TW008333, 2002).

With the pressing health needs of the Costa Rican population and lagging biomedical research development as a backdrop, over its 5-year span (2002-2007), the U.S./Costa Rica Psychiatric Genetics Research Training Program recruited and trained 7 long-term research fellows (1 to 3 years of training), all of whom returned to Costa Rica to create a well-educated and competent group of clinician/scientists able to carry out state-of-the-art research on psychiatric disorders, from the perspective of identifying the genes which contribute to these diseases. Among these research fellows were three Costa Rican psychiatrists, one Ph.D.-level psychologist, a Master’s-level psychologist, a Master’s-level genetic basic scientist, and a Baccalaureate who received additional training in statistical genetics. These fellows worked closely with research scientists and clinicians led by Dr. Michael Escamilla in San Antonio, Texas, and presented their work at a number of national and international meetings. Fellows continued their work at the University of Costa Rica, working with the psychiatric genetics research team led by Dr. Henriette Raventós and applying their newly learned skills to accomplish research work in mental health projects in Costa Rica. Among published articles from this group of fellows are articles identifying genes associated with schizophrenia, depressive symptoms, and diagnostic methodologies for psychiatric studies (Walss-Bass, Soto-Bernardini, Johnson-Pais, Leach, Ontiveros, Nicolini, Mendoza, Jerez, Dassori, Chavarria-Siles, Escamilla, & Raventos, 2009; Contreras, Hernández, Quezada, Dassori, Walss-Bass, Escamilla, & Raventos, 2010; Contreras, Dassori, Medina, Raventos, Ontiveros, Nicolini, Muñoz, & Escamilla, 2009).

In 2009, the Fogarty International Center awarded a new 5-year grant to train a new group of clinical researchers in neuropsychiatric genetics. This new grant is in place at the Center of Excellence in Neurosciences in the Paul L. Foster School of Medicine, Texas Tech University Health Sciences Center, and works with research fellows from Costa Rica who wish to gain further education and research experience in neuroscience. While allowing clinicians and scientists from Costa Rica the opportunity to gain skills in the field of psychiatric genetics research, the program also broadened to include work in other neurologic disorders (such as the dementias and epilepsy). In addition, the program also has a track for students who wish to pursue a Ph.D. degree in Pharmacology and Neurosciences. Since its inception in 2009, seven researchers from Costa Rica have matriculated to this program in Texas (there are two main research sites in Texas, one in El Paso and one in San Antonio, and the initial years of the Ph.D. program occur in Lubbock, Texas). These research fellows have included one psychiatrist, three Neurology residents, one psychologist, one Master's student in Biology, and one Master's-level student who is now in the Texas Tech University Health Sciences Center Ph.D. program. This new group of researchers has worked on projects including dementia, epilepsy, cerebrovascular disease, schizophrenia, substance use disorders (Jiménez-Castro, Raventós-Vorst, & Escamilla, 2011) and environmental stressors for psychiatric disease.

At the present time, the U.S./Costa Rica Neuropsychiatric Genetics Research Training Program is accepting applications from Costa Rican clinicians and scientists who are interested in furthering their education and ability to eventually conduct research in psychiatric and neurologic diseases in the Costa Rican population. A major challenge for all such researchers is to have institutional support or affiliations with a university or health service in Costa Rica, which will serve as a base for their research careers upon return to Costa Rica. Former fellows of these training programs are currently working at diverse institutions in Costa Rica, including the University of Costa Rica, the Seguro Social, and the Hospital Nacional Psiquiátrico in Pavas. It is our hope that current and former fellows

will serve as effective mentors for the next generation of Costa Rican clinicians and scientists during the current decade and beyond. The last 20 years have seen a number of important studies conducted in Costa Rica, which have identified risk genes for schizophrenia and bipolar disorder, and which involved fellows in these U.S.-Costa Rica training programs. We expect that the current group of fellows will play a key role in future discoveries not just in psychiatric disorders, but in neurologic diseases that affect the Costa Rican population. Accurate strategies to diagnose and treat these illnesses depend on researchers working within Costa Rica and working closely with clinicians and other health professionals in hospitals and clinics throughout the country. In addition, discoveries in Costa Rica may also help shed light on the mechanisms and biological and environmental causes of neuropsychiatric disorders that will help us understand these diseases as they apply to other Latino populations and the entire world. Costa Rican scientists and clinicians have made, and should continue to make, for generations to come, important contributions to the world scientific community.

As current members of the U.S./Costa Rica Neuropsychiatric Genetics Research Training program, we are grateful to have played a role in the development of the research community in Costa Rica over the last twenty years. We look forward to continuing our collaborations with the community of Costa Rican scientists and clinicians who are working to improve the treatment of persons who suffer from these serious mental and neurologic problems.

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