The Discovery of the Dardarin Gene 15 Years Later: A Globalized Local History

In Spain, the history of the discovery of *LRRK2* dates back to 1978, when José Félix Martí Massó identified the original aggregation of cases in a small valley of the Urola River in the heart of the Spanish Basque Country. In the absence of reliable historical medical records in a rural area, the preliminary examination of the first patients suggested that a pattern of a dominant trait with nearly complete penetrance indicated a possible genetic etiology of the disease. Clinically these patients were indistinguishable from other patients with sporadic Parkinson's disease with regard to the clinical picture, therapeutic response, and disease evolution. The hypothesis of a genetic origin of the disease had been postulated many years previously[1] with more recent reemphasis by some authors,[2] but it was falling into relative obscurity, especially after the publication of cases of toxic parkinsonism caused by 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine.[3] After Polymeropoulos and colleagues[4] discovered the synuclein gene in the Contursi kindred in the late 1990s, aided by the development of molecular biology tools, a true search for the causative gene could begin. The neurogenetics group in San Sebastián already had experience in searching for other genes, taking advantage of the relative genetic homogeneity of the Basque population and the relatively low geographic mobility of people from their original environments.

Coro Paisán was a young woman with a degree in biology from the University of Navarra who arrived at the laboratory of Adolfo López de Munain in 1999. She began initially in San Sebastián and subsequently in Valencia to study these Basque families and confirmed in 2002 that the locus coincided with that described by Funayama and colleagues.[5] That same year, Coro Paisán traveled with the Basque families to Bethesda, Maryland, where the search for the gene could be accelerated. One important fact that was a great advantage was that the Basque researchers had almost complete certainty that those families were in fact branches of a bigger single family. Thus, we arrive at the glorious days of October 2004 described in their letter by Singleton and Gasser from their personal perspectives, where both groups concluded that PARK8 was caused by mutations in a gene until then unknown, *LRRK2*, located on chromosome 12 (A.B. Singleton and T. Gasser, unpublished data, 2019). While the draft of our *Neuron* article was being written, José Félix Martí Massó and Adolfo López de Munain found that the gene name *LRRK2* was quite unpronounceable in Spanish or English and decided to christen the protein synthesized by *LRRK2* as dardarin. This name comes from the Basque word *dardara* that can be translated as *tremor* in English, indicating that this feature is a main symptom of a relatively benign form of Parkinson's disease. The word is a small tribute to the hundreds of affected individuals, patients and relatives, from a small community who collaborated to find this gene that we are sure contains the most important keys to explain the pathophysiology of Parkinson's disease.

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