THE DISCOVERY OF THE DARDARIN GENE 15 YEARS AFTER: A GLOBALIZED LOCAL HISTORY

By

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In Spain, the history of the discovery of *LRRK2* dates back to 1978, when José Félix Martí Massó, identifies the original aggregation of cases in in the environments of the 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 a dominant trait with nearly complete penetrance and therefore begins to turn to a possible genetic ethiology of the disease. Clinically these patients were indistinguishable from other patients with sporadic Parkinson's disease regarding clinical picture, therapeutic response and evolution. The hypothesis of a genetic origin of the disease had already been formulated many years ago[1] and rescued more recently by some authors[2], but it was falling into relative oblivion especially after the publication of cases of toxic parkinsonism caused by MPTP[3]. It was in the late 1990s, after Polymeropoulos discovered the synuclein gene in the Contursi kindred[4] and the generalization of molecular biology tools, when 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 relative 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, first in San Sebastián and then in Valencia, to study these Basque families, and confirmed in 2002 that the *locus* coincided with that described by Funayama[5]. That same year, Coro Paisán travelled with the Basque families to Bethesda where the search for the gene could be accelerated. One important fact that was a great advantage, as Andy Singleton recounts, was the fact 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 of that 2004 described in their letter by Andy Singleton and Thomas Gasser from their personal perspectives, where both groups conclude that PARK8 was caused by mutations in a gene until then unknown, *LRRK2*, located on chromosome 12[6]. While the draft of our Neuron paper was been 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 baptize the protein synthesized by LRRK2 as *dardarin* from the Basque word *dardara* that can be translated as *tremor* in English, indicating that this feature is main symptom of a form of Parkinson relatively benign. The word is a small tribute to the hundreds of affected individuals, patients and relatives, from a small community who contributed collaborated to find this gene that we are sure that contains the most important keys to explain the pathophysiology of Parkinson's disease.

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