GENETIC SCREENING OF THE GLUCOCEREBROSIDASE GENE IN SPANISH PARKINSON´S DISEASE PATIENTS REVEALS NOVEL MUTATIONS AND STRENGTHENS ITS ROLE IN LEWY BODY DISORDERS

N. Setó-Salvia1,2, H. Houlden3, J. Pagonabarraga1, B. Pascual-Sedano1, A. Campolongo1, I. Matas1, L. Muñoz1, O. Dols-icardo1, A. Tucci1, C. Paisán-Ruiz4, J. Hardy4, J. Kulisevsky1,5, J. Clarimón1,5

1Department of Neurology, Hospital Sant Pau, Barcelona, 2Institut Català de Paleoecologia Humana i Evolució Social (IPHES), Universitat Rovira i Virgili (URV), Tarragona, Spain, 3Molecular Neuroscience, UCL Institute of Neurology, 4Laboratory of Neurogenomics and Reta Lila Weston Laboratories, UCL. Institute of Neurology, London, UK, 5Center for Networker Biomedical Research in Neurodegenerative Diseases (CIBERNED), Madrid, Spain

Introduction: Mutations in glucocerebrosidase gene (GBA) are associated with Parkinson´s disease (PD) and dementia with Lewy bodies (LBD). The aim of our study was to determine the frequency of GBA mutations in the Spanish population in PD and LBD patients, and compare these frequencies with neurologically healthy elderly individuals.

Methods: We conducted a comprehensive sequencing analysis of the GBA gene in 228 patients with clinical diagnosis of PD, 17 pathologically confirmed LBD patients, and 190 controls from Barcelona, Spain.

Results: We found 22 PD patients carrying a mutation (9.6%), in comparison with only 1 control individual (0.5%) (OR = 20.2, \( P = 4.6 \times 10^{-5} \)). Among the LBD patients, we detected two mutations, one individual carrying the recombinant RecNcI allele and one brain with the common variant N370S (\( P = 2.0 \times 10^{-4} \)). The N370S and the L444P were the most frequent alterations, representing 22.7% and 27.2% of all mutations, respectively. We also found two novel mutations (L144V and S488T) and seven previously described mutations (M123T, G202R, I260T, T369M, W393R, D409H and RecNcI) in patients with PD.

Conclusion: This is the first comprehensive study of the GBA gene in the Spanish population. Our analysis supports the role of this gene in PD patients and suggests that sequencing of the entire gene is mandatory to perform a GBA mutation screening in Spanish population.