The expression of *ergic53* and *dMCFD2* in dopaminergic neurons interacts with rotenone exposure affecting dopaminergic neuron viability.

Póster

Genética y Genómica Molecular

Daniel Oropesa [1, 2], Francisco Salinas [1, 2], Gonzalo Olivares [2, 3], Paula Amado-Hinojosa [4], Javiera Avilés [1, 2], Jorge M. Campusano [4], Andrés Klein [5], Patricio Olguin [1, 2].

(1) Universidad de Chile, Instituto de Ciencias Biomedicas, Facultad de Medicina, Independencia 1027, Santiago, Chile.
(2) Universidad de Chile, Departamento de Neurociencia, Facultad de Medicina, Independencia 1027, Santiago, Chile.
(3) Universidad Mayor, Center for Integrative Biology, Facultad de Medicina y Ciencias de la Salud, Camino La Pirámide 5750, Santiago, Chile.
(4) Pontificia Universidad Católica de Chile, Departamento de Biología Celular y Molecular, Facultad de Ciencias Biológicas, Marcoleta 367, Santiago, Chile.
(5) Universidad del Desarrollo, Clínica Alemana, Centro de Genética y Genómica, Facultad de Medicina, Avenida Plaza 680, Santiago, Chile.

danieloropesa09@hotmail.com

Parkinson's disease (PD) is characterized by the progressive loss of dopaminergic neurons, causing motor and non-motor symptoms, most notably sleep disturbance. Gene-pesticide exposure interaction (GPEI) has been reported to play a key role in the etiology of PD. Notably, the exposure to rotenone, a mitochondrial complex I inhibitor, has been strongly associated with PD and causes Parkinson-like phenotypes in animal models. We have found that non-coding genetic variants in *ergic53* and in *dMCFD2* are associated with Gene-rotenone exposure interaction in sleep behavior.

Here, we aim to determine whether these non-coding genetic variants affect the function of *ergic53* and *dMCFD2,* and if the expression of these genes affects the viability of dopaminergic neurons in response to rotenone. We assessed the effect of a deletion comprising two nucleotides in the 3'UTR of *ergic53,* six SNPs and two

insertions localized in the Dorsal transcription factor binding site of *dMCFD2* third intron. Then we evaluated whether knockdown of these genes in dopaminergic neurons affects neuronal viability in response to rotenone.

Using a sleep monitoring system in Drosophila, we observed that these variations produce significant differences in daytime and nighttime sleep after exposure to rotenone. Furthermore, the decrease in ergic53 expression results in changes in the number of dopaminergic neurons in distinct clusters after rotenone exposure.

These findings suggest that knockdown of *ergic53* by RNAi produced differential changes in the population of dopaminergic neurons in rotenone-exposed versus unexposed neurons, pointing to these genes as potential mediators of pesticide-induced Parkinsonian-like phenotypes and candidates for functional studies.

Palabras Clave

(1) Parkinson's, (2) Drosophila, (3) Sleep, (4) non-coding genetic variants, (5) Dopaminergic.

Financiamiento:

ANID, FONDECYT Regular 1251006