Su Jin Noh et al., J Neurol Neurophysiol 2018, Volume 9
DOI: 10.4172/2155-9562-C4-070

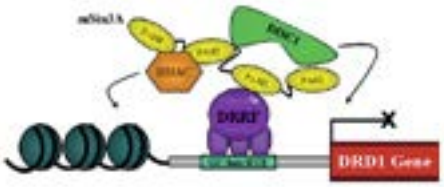
26th European Neurology Congress

August 06-08, 2018 | Madrid, Spain

DISC1-deficiency exaggerates cocaine sensitization by disrupting co-repressor complex DRRF-mSinA-DISC1 for *DRD1* gene

Su Jin Noh, Yeongjun Suh and **Sang Ki Park**
Pohang University of Science and Technology, Republic of Korea

Accumulating evidence suggest that disrupted-in-schizophrenia 1 (DISC1) modulates dopamine mediated function and involved in gene transcription in the brain. Our study was focused on these novel functions of DISC1 in the dopamine system. We demonstrated that DISC1-deficient mice showed an increase in dopamine D1 receptor (DRD1) transcripts in striatal region of the brain. DISC1-deficiency resulted in facilitation of the psychostimulant effect of cocaine in DISC1-deficient mice. The dopamine 1 antagonist, SCH-23390 blocked the psychostimulant effect of cocaine in DISC1-deficient mice. To elucidate molecular mechanism of this phenomenon, we characterized a novel co-repressor complex for *DRD1* gene locus composed of DRRF-mSin3A-DISC1. First, we could find a novel interaction between DISC1 and DRRF mainly co-localized in the nucleus. We also identified mSin3A binding with DRRF and DISC1, interestingly the binding intensity between DRRF and mSin3A was significantly increased by DISC1 co-expression. Furthermore, we observed an altered dopamine receptor mediated signaling in cultured striatal neurons (DIV 7) from DISC1-deficient mice. The basal level of cAMP and p-ERK were remarkably increased in DISC1 mutant mice. Taken together, we demonstrate a role of DISC1 in the striatum during cocaine sensitization, suggesting distinct mechanism of DISC1 in modulation of dopamine system through DRRF-mSinA-DISC1 co-repressor complex for *DRD1* gene.



Recent Publications

1. Shin K Y, Noh S J, Park C H, Jeong Y H, Chang K A, Yoo J, Kim H J, Ha S, Kim H S, Park H J, Lee H J, Moon C and Suh Y H (2016) Dehydroevodiamine•HCl protects against memory impairment and cerebral amyloid-beta production in Tg2576 mice by acting as a beta-secretase inhibitor. CNS Neurol Diord Drug Targets 15(8):935-944.
2. Ryu J, Zhang R, Hong B H, Yang E J, Kang K A, Choi M, Kin K C, Noh S J, Kim H S, Lee N H, Hyun J W and Kim H S (2013) Phloroglucinol attenuates motor functional deficits in an animal model of Parkinson's disease by enhancing Nrf2 activity. PLoS One 8(8):e71178.
3. Kopalli S R, Noh S J, Koppula S and Suh Y H (2013) Methylparaben protects 6-hydroxydopamine-induced neurotoxicity in SH-SY5Y cells and improved behavioral impairments in mouse model of Parkinson's disease. Neurotoxicology 34:25-32.
4. Kopalli S R, Koppula S, Shin K Y, Noh S J, Jin Q, Hwang B Y and Suh Y H (2012) SF-6 attenuates 6-hydroxydopamine-induced neurotoxicity: An *in vitro* and *in vivo* investigation in an experimental models of Parkinson's disease. J Ethnopharmacol 143(2):686-94.
5. Noh S J, Lee J M, Lee K S, Hong H S, Lee C K, Cho I H, Kim H S and Suh Y H (2011) SP-8203 shows neuroprotective effects and improves cognitive impairment in ischemic brain injury through NMDA receptor. Pharmacol Biochem Behav 100(1):73-80.

Biography

Su Jin Noh has her expertise in drug development and evaluation in neurological disorders. She studied potential drug development by mechanism-based targeting for curing neurodegenerative disease such as Alzheimer's disease, Parkinson's disease and stroke during her PhD program. Now she focuses on discovery of pathology of neuropsychiatric disease including schizophrenia or addiction.

sujin16@postech.ac.kr