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2. **Title**

   Nicotine-related Molecules in Neuropsychological Functions of Mood Disorders: Integrated Genetic Analysis between Clinical and Basic Studies

3. **Period**

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4. **Summary**

   The smoking incentive is considered as self-medication for own psychoses, including nicotine (NIC) dependence by stimulating nicotinic acetylcholine receptors (nAChRs) in the central nervous system of patients with psychiatric disorders, such as mood disorders and schizophrenia. However, the effects of NIC on the neuropsychological function and its molecular mechanisms are still unclear. We conducted comprehensive gene expression analysis between clinical and basic studies to elucidate the molecular functions of identified susceptibility genes of mood disorders. Repeated treatment with NIC (0.3 mg/kg) is useful and effective for stress-induced depressive-like behaviors without affecting reward systems. The remission of social behavior impairment by NIC may be mediated via regulating some intracellular signal-related molecules (Akt, CaMK II, and/or ERK1/2) in the hippocampus of stressed mice. In analysis of expression profiles between the lymphoblastoid cell line established from patients with depression and the prefrontal cortex or peripheral blood in mice exposed to defeat stress as juveniles, several genes were differentially expressed. Identified genes were involved in NIC reactivity and cholinergic neurotransmission by in silico analyses, suggesting that these genes are associated with pathophysiology of mood disorders and neuropsychiatric functions. The roles of NIC-related molecules associated with the pathophysiology of mood disorders and neuropsychiatric functions will be elucidated by evaluating the pharmacological actions of NIC using model mice. In addition, it is suggested that differentially expressed genes in both samples of model animal and human are applicable as peripheral biomarkers for social impairment of mood disorder.