1. No.
   2023G008

2. Title
   Mechanism for the Regulation on Neurotransmission by Hydrogen Sulfide and Polysulfides

3. Period
   2023-2025

4. Summary

   Hydrogen sulfide (H_2S) and polysulfides are produced by cystathionine β-synthase (CBS), cystathionine γ-lyase (CSE), 3-mercaptopyruvate sulfurtransferase (3MST), and these molecules are contained in cigarette smoke. H_2S/polysulfides modulate the release of neurotransmitters and protect neurons from oxidative stress including oxytosis and ferroptosis. The levels of these molecules in cigarette smoke are in the range of influencing the physiological activities of endogenous counterparts. The effects of these endogenous molecules as well as those in cigarette smoke were intensively studied. First year: The regulation of neurotransmitters releases and the induction of hippocampal long-term potentiation, a model of memory formation by both endogenous and exogenous H_2S/polysulfides, as well as the induction of schizophrenia-like behavior in 3MST-knockout rats were shown. Second year: We showed that the neuronal cells prepared from 3MST-knockout rats were sensitive to oxidative stress, while those from knockout of TRPA1 channels, which are the target of polysulfides, were resistant to oxidative stress. Final year: The levels of H_2S/polysulfides in cerebrospinal fluid and plasma obtained from the same individuals of schizophrenia, Alzheimer's disease, Parkinson's disease was compared to those of control individuals with or without smoking habits. We showed the possibility of palatability of schizophrenia patients to smoking and the lower risk of developing Parkinson's disease by smoking.