1. No.
   2021G026

2. Title
   Identification and functional analysis of presynaptic enhancers associated with nicotine addiction.

3. Period
   2021-2023

4. Summary
   Although much research has been conducted on the brain signal transduction associated with nicotine addiction at the cellular and the neuronal receptor levels, the presynaptic level has not been fully elucidated. One of the reasons is that a preparative method for biological samples has not been established, but in this study, we succeeded in establishing a preparative method of purified synaptic vesicles and a method of biochemical functional analysis. Using this method, we revealed significant differences in transmitter uptake. In particular, serotonin, dopamine, and noradrenaline are thought to be neurotransmitters that are released when nicotine binds to receptors. Therefore, in my final year, I focused on the structural analysis of VMAT2, which transports serotonin, dopamine, and noradrenaline to synaptic vesicles in the brain. We have revealed apo state, neurotransmitter or inhibitor bound states and have obtained structural insights on the multiple conformations of VMAT2. In the future, we believe that this structural analysis will lead to a biochemical analysis of why the research results obtained up to the second year.