1. No.
   2021G030

2. Title
   Novel drug development of refractory depression target for nicotinic acetylcholine receptor activation

3. Period
   2021-2023

4. Summary
   Calcium/calmodulin-dependent protein kinase IV (CaMKIV) null mice exhibit depressive-like behaviors, which do not improve following chronic treatment with the selective serotonin reuptake inhibitors (SSRIs) such as paroxetine. Here, we demonstrate that whether repeated administration of galantamine, a positive allosteric modulator at α7-type nAChR subtype, for 14 days improves depressive-like behaviors in CaMKIV null mice. Repeated administration of galantamine for 14 days improves depressive-like behaviors in CaMKIV null mice by tail-suspension task and forced-swim task. Consistent with behavioral observations, reduction of the intracellular Ca^{2+} signaling pathway and BDNF protein levels in DG were significantly rescued by the administration of galantamine. Recently, we have identified that Kir6.1 is an upstream regulator of CaMKIV signaling cascade. Therefore, we also demonstrate that whether repeated administration of paroxetine for 14 days improves depressive-like behaviors in Kir6.1 heterozygous mice. Unlike CaMKIV null mice, depressive- like behaviors in Kir6.1 heterozygous mice was ameliorated by the repeated administration of paroxetine.