1. **No.**

   FP01902053

2. **Title**

   Activation of the Non-neuronal Cardiac Cholinergic System Ameliorates Impairment of Glucose Metabolism and Angiogenesis in db/db Heart

3. **Period**

   2016-2020

4. **Summary**

   NNCCS plays a critical role not only in the homeostasis of cardiac functions including anti-ischemic potency through the modification of energy substrate preference in the heart, acceleration of angiogenesis, but also in the modification of the CNS functions through activation of the afferent vagus nerve, the terminal end of which is activated in the heart by NO synthesized by the NNCCS action. Furthermore, the modification of the CNS function by the NNCCS is partly mediated by upregulation of claudin-5, a responsible BBB component molecule. Therefore, BBB function is also dependent on the existence of the vagus nerve. Based on these mechanisms the NNCCS is involved in alteration of the CNS function, i.e., acceleration of the anti-stress like CNS phenotypes. The latter is represented by induction of anti-depressive, anti-aggression, and anti-anxiety reactions. NNCCS also induces anti-inflammatory responses in either a systemic or local manner, specifically in the vagus nerve-regulated organs, including the brain, spleen and the liver. Based on these results, the NNCCS, first expected as the heart-specific system, possesses multi-functions in the whole body through its cross-talk mechanisms, including immunological, neurological, and psychological effects.