1. No.
   2021G024

2. Title
   Central nervous system dysfunction by the extract of heated tobacco products is associated with blood-brain barrier breakdown

3. Period
   2021-2021

4. Summary
   Although heated tobacco products (HTPs), which allow inhalation of nicotine without burning, are expected to have less harmful chemicals induced by combustion than traditional cigarettes, it is unclear whether the use of HTPs increases the risk for cerebrovascular and neurological diseases with the blood-brain barrier (BBB) disruption. One of the HTPs distributed in Japan, Ploom TECH® was used. It heats a non-nicotine liquid at lower temperatures, which passes through granulated tobacco leaves, to produce nicotine-containing vapor. To mimic the vapor, we extracted granulated tobacco leaves in Ploom TECH® tobacco capsule with water at 60°C (Ploom TECH® tobacco extract; PTE). PTE mainly contains nicotine, but did not contain other compounds which are detected in the extract of traditional cigarette smoke. Male ICR mice (8 weeks old) were subcutaneously injected with 50% or 100% PTE (as 2.25 or 4.5 mg/kg/day of nicotine, respectively) for 7 days. We found that 100%PTE induced severe seizure convulsion with death. 50%PTE-treated mice exhibited moderate seizures and the increased [^{14}C]sucrose influx rate in the blood-to-brain direction. PTE decreased mRNA expression of Slc7a5, Abcb1a and Abcg2 in mouse brain endothelial cells. Therefore, the HTP-derived vapor would contain the substances which induce BBB dysfunction and seizures. Our results provide the possibility that the use of HTPs induces cerebrovascular and neurological adverse effects.