1. No.
   2022G031

2. Title
   Relationship between Brain Tissue Cerebral Vessels and Brain Tumors Caused by Extracts from Tobacco and Heated Tobacco Products

3. Period
   2022-2024

4. Summary

   We compared the cellular effects of cigarettes smoke extracts (CSE) from heated tobacco products, with nicotine and tar removal, to those of conventional tobacco. Using normal human astrocytes, human umbilical vein endothelial cells, and human oral cancer cells, we observed that CSE derived from conventional tobacco induced cytotoxicity at low concentrations. In contrast, CSE derived from heated tobacco products exhibited a biphasic effect, promoting cell proliferation at low concentrations while inducing cytotoxicity at high concentrations. Additionally, both heated tobacco products and conventional tobacco inhibited cell migration. We focused on cytotoxicity and identified its underlying mechanisms. We confirmed that both CSE of heated tobacco and conventional tobacco induce cell toxicity through apoptosis mediated by reactive oxygen species (ROS) and p38 activation. Furthermore, this process was associated with an increase in intracellular Ca^{2+} concentration and was found to be mediated by CaMKK2.

   In the future, we aim to identify the mechanisms by which CSE derived from heated tobacco products promote cell proliferation at low concentrations and conduct studies focusing on individual chemical compounds.