1. No.
   2020G019

2. Title
   Determining the Effects of Cigarette Smoking on Pancreatic Cancer Development and Generating Novel Therapeutics for Pancreatic Cancer Treatment

3. Period
   2020-2022

4. Summary

   Pancreatic cancer is one of the cancer types with the poorest patient prognosis. Smoking is one of the environmental factors that can influence the development of pancreatic cancer, but the precise role of smoking in the development of pancreatic cancer has not been elucidated.

   In this study, we sought to address this question by establishing and utilizing multiple experimental systems. First, we established a method to prepare cigarette smoke extracts by dissolving cigarette smoke in buffer solution. Next, they genetically engineered *Drosophila* to generate '4-hit flies' that mimic the 4-gene alterations of pancreatic cancer patients (*KRAS*, *TP53*, *CDKN2A*, and *SMAD4*), and found that administration of the extract to these flies increased their lethality. Furthermore, the applicant has established an assay to perform a comprehensive functional screening of all kinases in 4-hit flies and a platform to transplant human pancreatic cancer cells into mice. Using them, we demonstrated that the MEK inhibitor drug trametinib and the AURKB inhibitor BI-831266 are potential therapeutic candidates in the absence of cigarette smoke.

   In the future, we will continue to analyze whether these drug candidates can suppress pancreatic cancer traits in the presence of cigarette smoke. Through this, we aim to contribute to the improvement of human welfare.