1. No.
   2023Y001

2. Title
   To Investigate E-Cigarette–Induced Lung Cytotoxicity, Inflammation, and Fibrosis Using an Ex Vivo Precision-Cut Lung Slice (PCLS) System and an Induced-Usual Interstitial Pneumonia (iUIP) Mouse Model

3. Period
   2023-2025

4. Summary
   E-cigarettes are widely recognized as next-generation products and are considered a potentially safer than alternative to combustible cigarettes due to the absence of carcinogens, including nicotine and tar. In this study, we investigated the cytotoxicity of e-cigarette exposure on fibrotic lungs using an iUIP mouse model. E-cigarette (flavor, menthol, and CBD) aerosols were generated and bubbling through culture medium. In normal PCLS, CBD treatment significantly reduced cell viability, whereas no such effect was observed with flavor or menthol aerosol. The reduction in cell viability in iUIP PCLS was less pronounced than in normal PCLS. Cellular cytotoxicity in normal PCLS was significantly increased with CBD and flavor treatment. we focused on the effect of cytotoxicity in the normal lung PCLS treated with CBD. Numerous ROS-producing cells were observed in CBD-treated normal PCLS, but not in iUIP PCLS. CBD treatment induced mitochondrial dysfunction and detected numerous hypoxia probes in normal PCLS. This phenomenon was also observed in iUIP PCLS, however, iUIP PCLS already exhibited impaired mitochondrial function and showed less sensitivity to hypoxia. TUNEL positive cells significantly increased in normal PCLS treated with CBD, but not in iUIP PCLS. Therefore, CBD treatment may induce excessive oxidative stress, which is thought to have caused the numerous cell death observed in normal PCLS. This study indicates that young and healthy lungs are more susceptible to toxicity and cell death from exposure to CBD than fibrotic lungs.