1. No.
   2020G017

2. Title
   Identification of proinflammatory roles of smoking in pancreas

3. Period
   2020-2023

4. Summary
   Treatment with glutaminase inhibitors decreased cell viability of cell line with constitutive Nrf2 activation, and treatment with DEM, an Nrf2 activator, rendered the wild-type pancreatic cancer cell line sensitive to glutaminase inhibitor CB-839. Nrf2 activation in pancreatic cancer cells led to dependence to glutamate. The human pancreatic stellate cell line was more resistant to the glutaminase inhibitor, CB-839, compared to the hepatic stellate cell line. Immortalized human pancreatic stellate cell line, primary cultured pancreatic stellate cells, and LX2 cell line showed increased expression of Nrf2 target molecules, Nqo1 and xCT, by diethyl maleate treatment. Nrf2 activation sensitized the immortalized human pancreatic stellate cell line and primary cultured pancreatic stellate cells to CB-839. HO-1 expression in stromal cells was detected in pancreatic intraepithelial neoplasm (PanIN)-surrounding cells. PanIN-forming cells expressed xCT. Spink1 CKO mouse showed increased expression of HO-1 in pancreatic acinar cells. CB-839 pretreatment did not exacerbate caerulein-induced pancreatitis. The TRPV6 inhibitor, 2-APB, reduced cellular viability of human pancreatic cancer cell lines accompanied by survivin repression. Reduction of survivin was due to increased degradation by proteasome.