Supplementary Materials

Metabolic profiling

Untargeted metabolomics of pancreatic cyst fluid was performed using LC-MS (0.2 mL cyst fluid). Briefly, 100 µL of cyst fluid sample was mixed with 400 µL of extraction solvent (methanol: acetonitrile: acetone, 1:1:1 by volume) and incubated at -20°C for 1 hour followed by centrifugation (15,000 rpm for 10 minutes). The supernatant was transferred to a new tube and nitrogen dried. The samples were then reconstituted in 100 µL of reconstitution solvent (methanol: H_2O, 2:98), vortexed, and centrifuged before transferred to an autosampler vial with insert. 1290 Infinity Binary LC system from Agilent was used for chromatographic separation together with Waters Acquity UPLC HSS T3 1.8 µm 2.1 x 100 mm column in connection with a Water Acquity UPLC HSS T3 1.8 µm VanGuard pre-column. The detailed parameters were: data acquisition time 27 min, system equilibration time: 7 min, total run length: 34 min, flow rate: 0.45 ml/min, solvent A: 0.1% formic acid in water, solvent B: 0.1% formic acid in methanol, and column temperature: 55ºC. Same chromatographic method was used for both positive and negative mode. Mass spectrometer settings were as follows: ion source: gas temperature - 325 ℃, drying gas flow - 10 l/min, nebulizer pressure - 45 psig, sheath gas temperature - 400 ℃, sheath gas flow - 12 l/ml, capillary voltage - 4000 V, fragmentor voltage - 140 V, skimmer voltage - 65 V, mass range 50-1000 m/z, acquisition rate 2 spectra/s. Inline mass calibration was performed using debrisoquine sulfate (m/z 176.1182) and HP-0921 from Agilent (m/z 922.0098) in positive mode and 4-NBA (m/z 166.0146) and HP-0921 from Agilent (m/z 966.0007, formate adduct) in negative mode.