Differentiation of multiple types of pancreatico-biliary tumors by molecular analysis of clinical specimens.

Abstract:
Timely and accurate diagnosis of pancreatic ductal adenocarcinoma (PDAC) is critical in order to provide adequate treatment to patients. However, the clinical signs and symptoms of PDAC are shared by several types of malignant or benign tumors which may be difficult to differentiate from PDAC with conventional diagnostic procedures. Among others, these include ampullary cancers, solid pseudopapillary tumors, and adenocarcinomas of the distant bile duct, as well as inflammatory masses developing in chronic pancreatitis. Here, we report an approach to accurately differentiate between these different types of pancreatic masses based on molecular analysis of biopsy material. A total of 156 bulk tissue and fine needle aspiration biopsy samples were analyzed using a dedicated diagnostic cDNA array and a composite classification algorithm developed based on linear support vector machines. All five histological subtypes of pancreatic masses were clearly separable with 100% accuracy when using all 156 individual samples for classification. Generalized performance of the classification system was tested by 10 × 10-fold cross validation (100 test runs). Correct classification into the five diagnostic groups was demonstrated for 81.5% of 1,560 test set predictions. Performance increased to 85.3%
accuracy when PDAC and distant bile duct carcinomas were combined in a single diagnostic class. Importantly, overall sensitivity of detection of malignant disease was 92.2%. The molecular diagnostic approach presented here is suitable to significantly aid in the differential diagnosis of undetermined pancreatic masses. To our knowledge, this is the first study reporting accurate differentiation between several types of pancreatoco-biliary tumors in a single molecular analytical procedure.