Abstract:

The identification and characterization of precursor lesions is fundamental to develop screening programs for early diagnosis and treatment, aiming at reducing cancer-related mortality. Pancreatic ductal adenocarcinoma (PDAC) is an aggressive disease that becomes clinical apparent only in advanced stages. In order to enable screening procedures for early detection of PDAC, an exact characterization of precursor lesions is of utmost importance. Pancreatic intraepithelial neoplasias (PanIN) are the most frequent and best characterized precursors of PDAC and are lesions with a ductal phenotype thus indicating a ductal cell origin of PDAC. However, evidence from genetically engineered mouse models suggests that tubular complexes (TC) originating through a process of acinar-ductal metaplasia (ADM) form atypical flat lesions (AFL) that may represent an alternative pathway of pancreatic carcinogenesis. Based on a thorough morphological and genetic analysis of murine TC, AFL and PanIN and their human counterparts, anew dual model of pancreatic carcinogenesis is proposed taking into account the role of AFL as possible new precursors of PDAC.