Energy metabolism and proliferation in pancreatic carcinogenesis.

Abstract:
Pancreatic ductal adenocarcinoma (PDAC) is an aggressive cancer entity with a high proliferative potential. Uncontrolled cell proliferation is mediated by a number of core signaling pathways. Recently, novel data of PDAC biology suggest that these core signal pathways affect cell proliferation and metabolism simultaneously. Here, we reviewed the literature on core metabolic signaling pathways in pancreatic carcinogenesis. Results obtained from mouse genetics and in vitro experiments have demonstrated the significance of the Kras, p53, c-Myc, and Lkb1 networks in the proliferation of pancreatic epithelial and cancer cells. At the same time, these major pathways also affect energy metabolism by influencing glucose and glutamine utilization. In particular, Kras-mediated metabolic changes seem to be directly involved in carcinogenesis. However, there is a lack of solid evidence on how metabolism and proliferation are connected in pancreatic carcinogenesis. Understanding early and subtle changes in cellular metabolism of pancreatic epithelial-and specifically of acinar-cells, which accompany or directly influence malignant transformation and uncontrolled proliferation, will be paramount to define novel imaging and other modalities for earlier detection of PDAC.