Abstract

Pancreatic ductal adenocarcinoma (PDAC) is an extremely aggressive neoplasm, predicted to become the second leading cause of cancer-related deaths before 2030. This dismal trend is mainly due to lack of effective treatments against its metastatic behavior. Therefore, a better understanding of the key mechanisms underlying metastasis should provide new opportunities for therapeutic purposes. Genomic analyses revealed that aberrations that fuel PDAC tumorigenesis and progression, such as SMAD4 loss, are also implicated in metastasis. Recently, microRNAs have been shown to play a regulatory role in the metastatic behavior of many tumors, including PDAC. In particular, miR-10 and miR-21 have appeared as master regulators of the metastatic program, while members of the miR-200 family are involved in the epithelial-to-mesenchymal switch, favoring cell migration and invasiveness. Several studies have also found a close relationship between cancer stem cells (CSCs) and biological features of metastasis, and the CSC markers ALDH1, ABCG2 and c-Met are expressed at high levels in metastatic PDAC cells. Emerging evidence reveals that exosomes are involved in the modulation of the tumor microenvironment and can initiate PDAC pre-metastatic niche formation in the liver and lungs. In this review, we provide an overview of the role of all these pivotal factors in the metastatic behavior of PDAC, and discuss their potential exploitation in the clinic to improve current therapeutics and identify new drug targets. © 2017 Elsevier Ltd.