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I recently submitted the thesis about the work I performed as a PhD student in the Gavalas lab (Paul Langerhans Institute Dresden). There, I focus on the identification of novel cell populations with tumor-initiating capacity for pancreatic ductal adenocarcinoma (PDAC). PDAC remains among the most lethal malignant neoplasms, partly because most patients present either locally advanced disease or metastasis, and current first-line treatments are not particularly effective. The discovery of requirements for PDAC formation and the identification of the tumor initiating cells (TICs) would provide novel targets for chemotherapy that could help reduce its mortality. In previous work, we identified a mitochondrial enzyme, aldehyde dehydrogenase 1 family member B1 (Aldh1b1), that marks a specific centroacinar progenitor population in the adult mouse pancreas. Aldh1b1+ centroacinar cells are enriched in Kras expression, the main driver for PDAC, and strikingly, Aldh1b1 function is required for PDAC formation in a mouse model of the disease. To investigate whether Aldh1b1-expressing cells in the adult mouse pancreas can act as TICs, I have induced the expression of oncogenic Kras (Kras*) in Aldh1b1+ cells, have expanded them in vitro, and have been transplanted in the pancreas of immunocompromised mice. Nine months after transplantation, Kras*-expressing Aldh1b1+ cells induced the formation of neoplastic lesions in the host pancreas, suggesting that these cells have the capacity to initiate PDAC. To assess their tumorigenic potential in vivo, I have also generated a double-conditional mouse model that enables the activation of Kras* expression specifically in pancreatic Aldh1b1-expressing cells in a time-controlled manner. Since Aldh1b1 function is essential for PDAC initiation, I aimed to elucidate the metabolic role of Aldh1b1 in enabling tumor formation. Using a loss-of-function approach we have found that Aldh1b1 helps maintaining lower reactive oxygen species (ROS) levels in pancreatic progenitors during development. To discover whether Aldh1b1 also controls ROS levels during tumorigenesis, I am treating PDAC mouse models in an Aldh1b1null genetic background with a ROS scavenger. The restoration of tumor formation in the absence of Aldh1b1 would link the pro-tumorigenic function of Aldh1b1 to the maintenance of permissive ROS levels.