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Titel des Beitrags: Pancreatic cancers require autophagy for tumor growth.

Abstract:
Macroautophagy (autophagy) is a regulated catabolic pathway to degrade cellular organelles and macromolecules. The role of autophagy in cancer is complex and may differ depending on tumor type or context. Here we show that pancreatic cancers have a distinct dependence on autophagy. Pancreatic cancer primary tumors and cell lines show elevated autophagy under basal conditions. Genetic or pharmacologic inhibition of autophagy leads to increased reactive oxygen species, elevated DNA damage, and a metabolic defect leading to decreased mitochondrial oxidative phosphorylation. Together, these ultimately result in significant growth suppression of pancreatic cancer cells in vitro. Most importantly, inhibition of autophagy by genetic means or chloroquine treatment leads to robust tumor regression and prolonged survival in pancreatic cancer xenografts and genetic mouse models. These results suggest that, unlike in other cancers where autophagy inhibition may synergize with chemotherapy or targeted agents by preventing the up-regulation of autophagy as a reactive survival mechanism, autophagy is actually required for tumorigenic growth of pancreatic cancers de novo, and drugs that inactivate this process may have a unique clinical utility in treating pancreatic cancers and other
malignancies with a similar dependence on autophagy. As chloroquine and its derivatives are potent inhibitors of autophagy and have been used safely in human patients for decades for a variety of purposes, these results are immediately translatable to the treatment of pancreatic cancer patients, and provide a much needed, novel vantage point of attack.

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