Genome-wide genetic and epigenetic analyses of pancreatic acinar cell carcinomas reveal aberrations in genome stability.

Abstract:
Pancreatic acinar cell carcinoma (ACC) is an aggressive exocrine tumor with largely unknown biology. Here, to identify potential targets for personalized treatment, we perform integrative genome-wide and epigenome-wide analyses. The results show frequently aberrant DNA methylation, abundant chromosomal amplifications and deletions, and mutational signatures suggesting defective DNA repair. In contrast to pancreatic ductal adenocarcinoma, no recurrent point mutations are detected. The tumor suppressors ID3, ARID1A, APC, and CDKN2A are frequently impaired also on the protein level and thus potentially affect ACC tumorigenesis. Consequently, this work identifies promising therapeutic targets in ACC for drugs recently approved for precision cancer therapy.