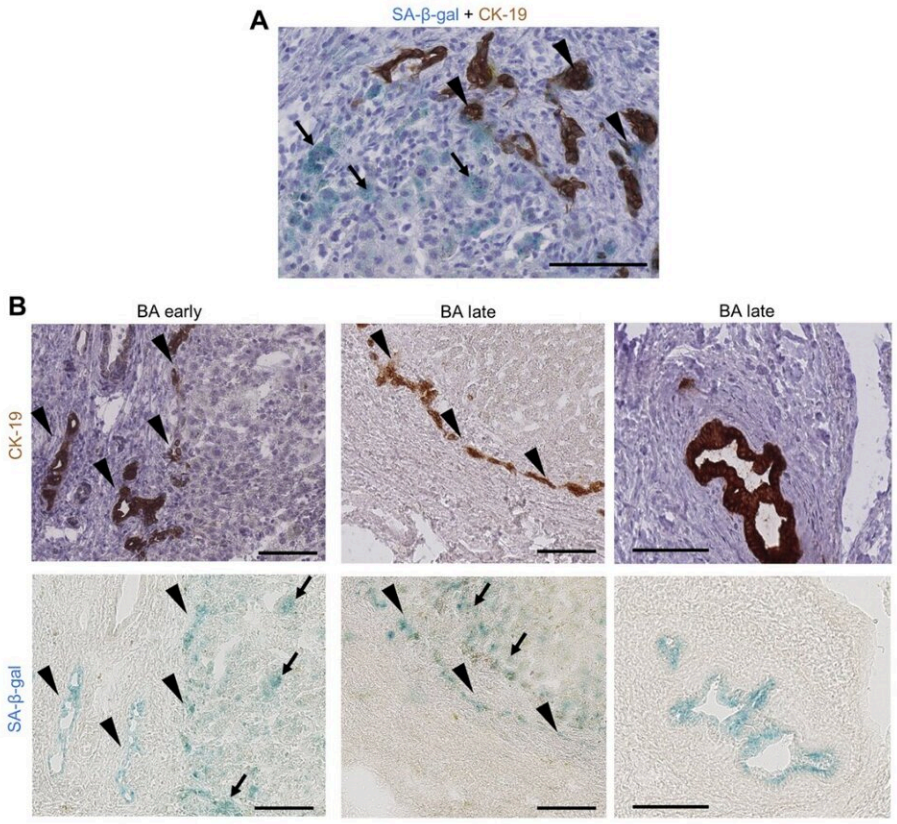
Medical Xpress

Senescence and senotherapies in biliary atresia and biliary cirrhosis

June 28 2023



Cholangiocytes and perinodular hepatocytes display cellular senescence in BA livers. Credit: *Aging* (2023). DOI: 10.18632/aging.204700

A new research paper titled "Senescence and senotherapies in biliary atresia and biliary cirrhosis" has been published in *Aging*.

Premature senescence occurs in adult hepatobiliary diseases and worsens the prognosis through deleterious liver remodeling and hepatic dysfunction. Senescence might also arise in biliary atresia (BA), the first cause of pediatric liver transplantation. Alternatives to transplantation are needed. In this new study, researchers from the Université catholique de Louvain in Brussels, Belgium, aimed to investigate premature senescence in BA and to assess senotherapies in a preclinical model of biliary cirrhosis.

"As there is a need for new therapies to avoid or delay liver transplantation in pediatric biliary cirrhosis, the aim of our work was to investigate premature senescence in BA through a multi-technical approach and to assess senotherapies in a preclinical model of biliary cirrhosis," the researchers write.

BA liver tissues were prospectively obtained at hepatoportoenterostomy (n=5) and liver transplantation (n=30) and compared to controls (n=10). Senescence was investigated through spatial whole transcriptome analysis, SA-β-gal activity, p16 and p21 expression, γ-H2AX and senescence-associated secretory phenotype (SASP). Human allogenic liver-derived progenitor cells (HALPC) or dasatinib and quercetin (D+Q) were administrated to two-month-old Wistar rats after bile duct ligation (BDL).

Advanced premature senescence was evidenced in BA livers from early stage and continued to progress until liver transplantation. Senescence and SASP were predominant in cholangiocytes, but also present in surrounding hepatocytes. HALPC but not D+Q reduced the early marker of senescence p21 in BDL rats and improved biliary injury (serum γGT and Sox9 expression) and hepatocytes mass loss (Hnf4a).

The researchers conclude, "BA livers displayed advanced cellular senescence at diagnosis that continued to progress until liver

transplantation. HALPC reduced early senescence and improved liver disease in a preclinical model of BA, providing encouraging preliminary results regarding the use of senotherapies in pediatric biliary cirrhosis."

More information: Giulia Jannone et al, Senescence and senotherapies in biliary atresia and biliary cirrhosis, *Aging* (2023). DOI: 10.18632/aging.204700

Provided by Impact Journals LLC