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**Longitudinal paired liver biopsies and transcriptome profiling in alcohol-associated hepatitis reveal dynamic changes in cellular senescence**

Rodrigo-Torres D, Kilpatrick A, Ferreira-Gonzalez S*, et al.* Longitudinal paired liver biopsies and transcriptome profiling in alcohol-associated hepatitis reveal dynamic changes in cellular senescence. *Gut* 2025; 74:1500-1513. doi: 10.1136/gutjnl-2024-334094

Alcohol associated hepatitis (AH) is an acute manifestation of alcohol-related liver disease which presents with jaundice, elevated liver enzymes and is characterised histologically by steatosis, inflammation and cell death (usually apoptosis). Senescence is a state where cells stop dividing and secrete pro-inflammatory factors, which has been shown to play a role in a range of acute and chronic liver disease. However, the role of senescence in AH is not well understood.

Rodrigo-Torres *et al.,* performed transcriptomic analysis of paired transjugular liver biopsies from day 0 and day 28 post-treatment of patients (n=27) with AH participating in the IL-1 Signal Inhibition In Alcoholic Hepatitis (ISAIAH) clinical trial with either placebo or canakinumab (IL-1 (interleukin-1) inhibitor).

Through bulk ribonucleic acid (RNA) sequencing they found downregulation of senescence markers as well as markers of senescence-associated secretory phenotype (SASP) – a group of proteins associated with senescence that drive inflammation at day 28 compared to day 0 associated with clinical resolution of AH. There was similar downregulation of apoptosis-associated factors. They additionally found upregulation of hepatocyte markers as AH resolved

Re-analysis of other AH datasets confirmed upregulation of senescence markers in AH compared to normal liver along with downregulation of hepatocyte markers. For further validation they used an *in vitro* model of hepatocytes and found that treating the cells with ethanol led to a transcriptomic increase in senescence markers by RNA sequencing.

Rodrigo-Torres *et al.,* concluded that senescence in AH may play a role in pathogenesis and the dynamic nature highlights it as a potential therapeutic target to modify the progression of disease.