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# Scientists reverse mechanism of fatty liver disease

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Researchers have identified the mechanism which causes a build-up of fat in the liver in a disease affecting one in five in the UK—and were able to reverse it in a mouse model.

People with Non-Alcoholic Fatty Liver Disease (NAFLD) develop excess fat in the liver even though they drink little or no alcohol. The condition can range from simple fatty liver to fibrosis and cirrhosis, and can ultimately lead to liver cancer.

A group of international researchers publishing today in the journal *Nature Communications*, report that senescent or old cells in the liver store excessive fat because mitochondria, the batteries of the cells, become damaged and cannot effectively use the fat as a source of fuel, resulting in its storage.

## Reversing the process

Researchers from the Newcastle University Institute for Ageing, UK, in collaboration with researchers from the Mayo Clinic, USA, and the Erasmus Medical Centre, in the Netherlands, used pharmacological and genetic approaches to "kill-off" senescent cells from mice, to decrease the build-up of unwanted fat in the liver and restore liver function to normal.

Dr Diana Jurk from Newcastle University's Institute for Ageing, who

leads the research team, said: "This is the first time that we have an effective therapy for fatty liver disease. Our discovery shows that by using this new method that can kill senescent cells, we may be able to make a significant impact in dealing with this very common life-threatening disease.

"While our approach worked in laboratory mice, we hope in the near future to be able to test these interventions in humans and potentially make a positive impact on people's lives."

## Method

The team used two separate methods to eliminate senescent cells; firstly by using a genetically engineered mouse in which senescent, worn-out cells can be "killed-off" and secondly by a treatment with a combination of the drugs—dasatinib and quercetin (D+Q)—known to specifically kill senescent cells.

Both approaches were equally successful in reducing the build-up of fat in the liver caused by a high fat diet or ageing in mice.

Mikolaj Ogrodnik, PhD student within the Institute for Ageing and lead author on the paper, said: "We are witnessing a very exciting time in ageing research. Scientists have realised that senescent cells are the cause of many diseases and we now have a way to fight them off."

Dr Jurk adds: "As we age we accumulate cell damage and we have shown that these older cells are storing excess fat due to their inefficient mitochondria. What is exciting is that we have been able to reverse this damage in mice by removing these older, worn-out cells, which opens the door to a potential cure."

The work has been funded by the BBSRC and Newcastle University's

Institute for Ageing.

The team are now intending to further their research by examining how the technique can be developed as a potential clinical treatment.

**More information:** Cellular senescence drives age-dependent hepatic steatosis. Mikolaj Ogrodnik et al. Cellular senescence drives age-dependent hepatic steatosis. *Nature Communications*. DOI: 10.1038/ncomms15691

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