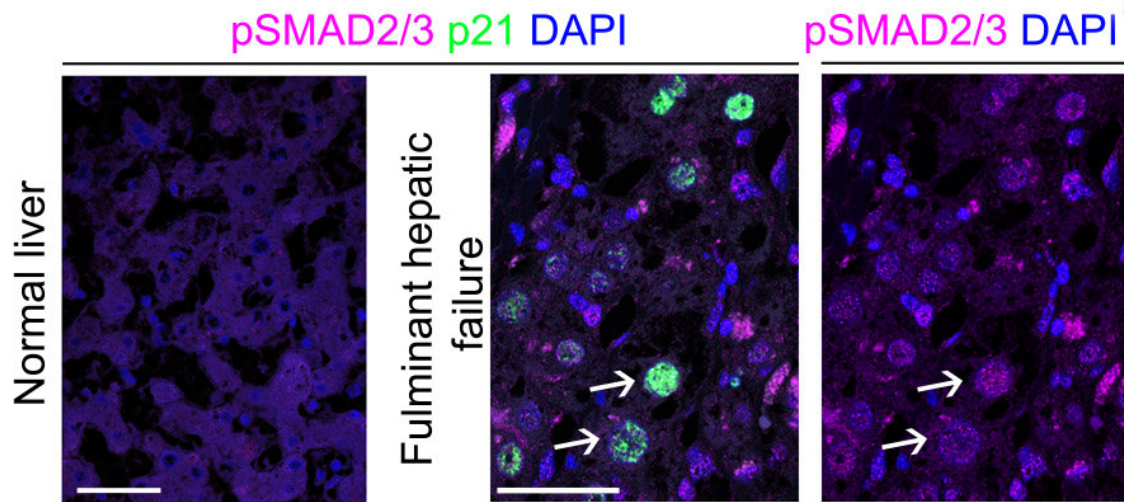


Anticancer drug offers potential alternative to transplant for patients with liver failure

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Microscopy images comparing a normal liver to a liver from a patient with liver failure due to an overdose of acetaminophen. The green and pink colors correspond to expression of the p21 and pSMAD2/3 proteins, respectively, while the white arrows indicate senescent liver cells. Credit: T.G. Bird et al., *Science Translational Medicine* (2018)

Patients suffering sudden liver failure could in the future benefit from a new treatment that could reduce the need for transplants, research published today shows.

Acute Liver Failure occurs when a healthy liver is so seriously damaged

it can no longer regrow and recover, leaving patients in urgent need of transplant.

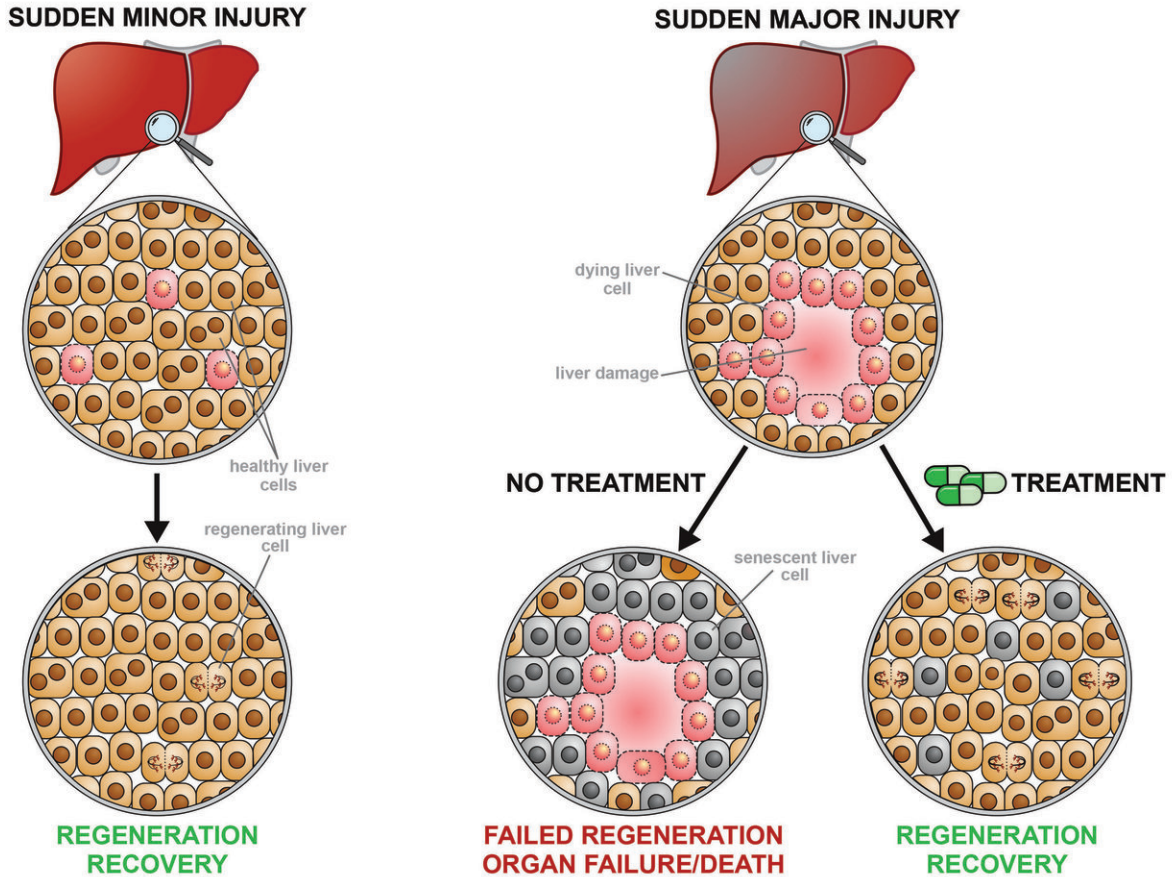
The liver helps support almost every other organ, by removing toxins, as well as making and storing the proteins and energy sources the body requires.

Often the damaged liver can regrow and recover on its own, but when it suffers massive injury, regeneration may fail and even 24 hours without a fully working liver can be life-threatening.

Paracetamol overdose is the most common cause of Acute Liver Failure, with around 200 UK and 2,000 US life threatening cases each year.

Researchers are, however, hopeful a therapy to prevent the need for liver transplant may now be possible following investigations to discover why and how the liver loses its natural ability to regenerate.

In a study in mice by researchers at the University of Edinburgh MRC Centre for Regenerative Medicine and the Cancer Research UK Beatson Institute in Glasgow, published in *Science Translational Medicine*, found liver injury, triggers a process—called senescence—usually associated with aging or chronic disease.



Inhibiting cellular senescence caused by acute liver injury improves liver regeneration. Credit: Dr M Müller

Using a class of drugs being developed as anti-cancer therapy to block the spread of this process, the researchers found that in mouse models the organ was able to regenerate after treatment, preventing death from liver injury.

Liver specialist Dr. Tom Bird, a Wellcome Trust Fellow, who led the study said: "Through our research so far we have identified a potential treatment for [acute liver failure](#), which may prevent the need for transplant. Most of the patients we see with this type of critical [liver](#)

[injury](#) are otherwise physically healthy, and have accidentally or, often, sadly, intentionally taken an overdose of paracetamol. While transplant offers incredible life-saving opportunities for these patients, it does mean a major operation and a lifetime of medication and with around 300 adults and children in the UK in need of a [liver transplant](#) at any one time, it cannot be guaranteed. New treatments like this which set liver regeneration free and may prevent the need for liver transplants, would make a huge difference for these patients. They may also allow us to use the livers available for transplantation for other patients with different forms of liver disease who might otherwise die whilst waiting for a suitable liver donor."

Further studies are now needed and the next step is to explore the potential of the new drugs in the clinic on patients with liver [failure](#).

Healthy livers can also fail due to infection by some Hepatitis viruses and recreational drug use—but were not the focus in this research.

Lindsay Keir, of Wellcome's Clinical and Physiological Sciences team said: "This important study offers hope to patients who develop sudden [liver failure](#) after taking too much paracetamol. Since this study was predominately carried out in mice, further research is needed before this could be used to routinely treat [patients](#). However, the research so far suggests that a medication could be used to treat this condition avoiding the need for a [liver](#) transplant which is a major operation and reducing the demand on the limited supply of livers available for [transplant](#)."

More information: T.G. Bird et al., "TGF β inhibition restores a regenerative response in acute liver injury by suppressing paracrine senescence," *Science Translational Medicine* (2018).

stm.sciencemag.org/lookup/doi/.../scitranslmed.aan1230

Provided by Wellcome Trust

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