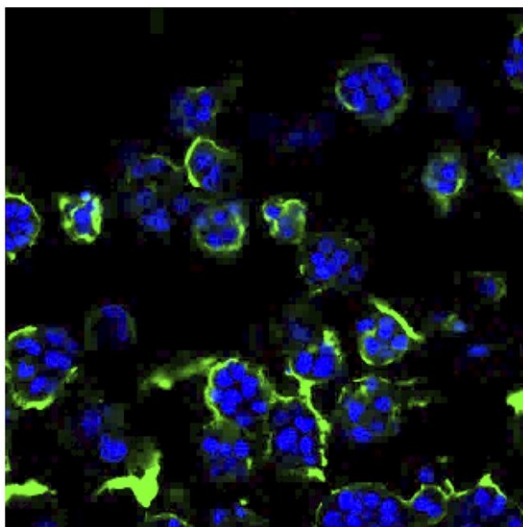


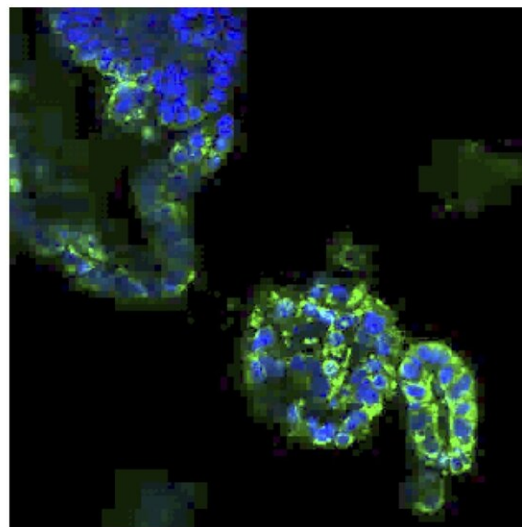
# New 3-D cultured cells mimic the progress of NASH

April 1 2020

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**Collagen I**



**$\alpha$ -smooth muscle actin**

Left panel: Expression of Collagen I protein in green indicates that fibrosis, one of the NASH characters, is formed in the NASH organoids. DAPI staining in blue shows nuclei of cells. Right panel: Expression of alpha-Smooth muscle actin protein in green indicates that hepatic stellate cells were activated in the NASH organoids. This also represents one of the NASH characters. Credit: T. Usui / TUAT

A research team led by scientists from Tokyo University of Agriculture

and Technology (TUAT), Japan, has successfully established 3-D cultured tissue that mimics liver fibrosis, a key characteristic of non-alcoholic steatohepatitis (NASH). For making the 3-D culture, cells were collected from liver tissues of NASH model mice. Their findings open up an alternative avenue for developing drugs for NASH patients, identifying new markers for early diagnosis, and better understanding the disease progression. Their findings were published in *Biomaterials* on Jan 27th, 2020.

In Japan, about 10 million people (8% of the population) are thought to carry NASH or to be at high risk for NASH. In the USA, a ballpark estimate indicates about 3% to 12% of adults have NASH. The NASH patients develop fatty liver regardless of alcohol intake and progress to liver cirrhosis or ultimately liver cancer. NASH symptoms include liver tissue inflammation, fat deposition, and fibrosis. Unfortunately, there are no medications available for treating NASH—hence its status as a major social problem.

In general, to test which drugs could cure NASH, researchers fed experimental animals a NASH-inducing diet followed by certain drugs. It is, however, obvious that using experimental animals to test drugs is not practical. "To mimic NASH in a dish, we started three-dimensionally growing cells that were collected from liver tissues of NASH model mice," said Dr. Tatsuya Usui, corresponding author of the paper, Senior Assistant Professor, Laboratory of Veterinary Pharmacology, Department of Veterinary Medicine, Faculty of Agriculture, TUAT. "These cells successfully grew in a dish and formed mini-organs called organoids."

For producing NASH organoids in a dish, we used cells from the liver of NASH mice with 3 different disease stages, such as the early stage (fatty liver), the middle stage ([fatty liver](#)), and the late stage (advanced fibrosis). The organoids were examined by standard histology methods,

such as HE staining, oil red staining, and Masson's trichrome staining to visualize cell shapes, oil production in cells, and connective tissues, respectively. In addition, immuno-staining, quantitative PCR, and RNA-sequencing were performed to visualize localization and amounts of bio-markers.

"After careful scientific analyses, we found that these [cells](#)' characters in the organoids were very similar to those of NASH [liver](#) tissues. Interestingly our NASH organoids also mimic the characters of these stages. We therefore concluded that NASH was reproduced in a dish using the [organoid](#) culture method for the first time," Usui explained. "We expect that drug discovery targeted for each stage can be done using these organoids. In addition our RNA-sequencing analysis found that several genes were elevated at all stages of organoids and some others were highly expressed at a specific state (patent application filed). So far, no effective diagnostic bio-markers have been found that accurately reflects the degree of progression of the NASH. Therefore, we expect that new reliable bio-markers for diagnosis can be identified using our NASH organoids," added Usui.

**More information:** Mohamed Elbadawy et al, Efficacy of primary liver organoid culture from different stages of non-alcoholic steatohepatitis (NASH) mouse model, *Biomaterials* (2020). [DOI: 10.1016/j.biomaterials.2020.119823](#)

Provided by Tokyo University of Agriculture and Technology

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