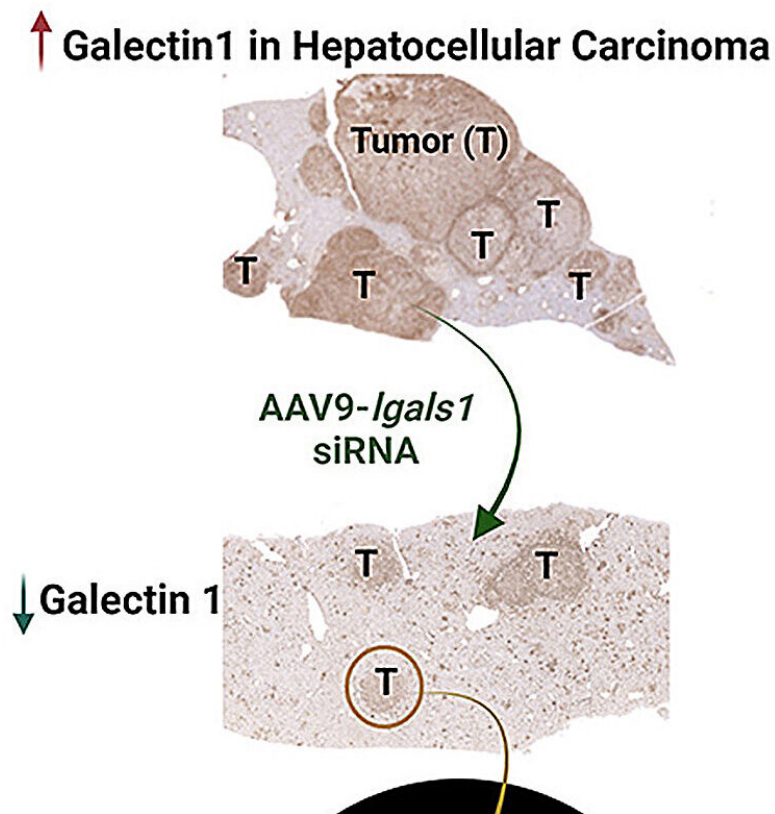


Scientists find gene therapy reduces liver cancer in animal model

November 30 2023, by Josh Baxt



Graphical abstract. Targeting Gal1 is effective in preventing as well as treatment of HCC and has translational potential.

Researchers at UC Davis Comprehensive Cancer Center have shown that inhibiting a specific protein using gene therapy can shrink hepatocellular

carcinoma (HCC) in mice. Silencing the galectin 1 (Gal1) protein, which is often over-expressed in HCC, also improved the anti-cancer immune response and increased the number of killer T cells inside tumors. The [study](#) was published in *Acta Pharmaceutica Sinica B*.

"We've long known that Gal1 is a biomarker for [hepatocellular carcinoma](#)," said Yu-Jui Yvonne Wan, a distinguished professor in the Department of Pathology and Laboratory Medicine and senior author of the study. "Gal1 expression in normal tissue is quite low and increases with [fatty liver disease](#), inflammation, and liver carcinogenesis. Now, we can see that Gal1 is more than a biomarker—it's a potential therapeutic target."

HCC, a [cancer](#) that starts in the liver, is one of the world's most common cancers. And the numbers are increasing, with incident rates more than tripling since the 1980s. The disease can also be quite deadly: In advanced stages, the five-year survival rate is less than 20%.

The Wan lab has spent decades studying liver diseases; this study builds on previous research.

Gal1 overexpressed in HCC

Gal1 suppresses the immune system from attacking healthy tissue. However, when it is overly expressed in HCC, it promotes cancer growth and keeps the immune system from attacking the tumor. In this study, the team found high Gal1 levels were associated with aggressive disease progression and poor survival. This link between increased Gal1 and poor outcomes has also been observed in HCC patients.

Earlier this year, the Wan group used [gene therapy](#) to increase microRNA-22 (miR-22), a non-coding RNA that regulates [gene expression](#), to study its impact on [liver cancer](#). This approach, led by

Ying Hu, an assistant professional researcher in Wan's lab, showed miR-22 overexpression reduced liver inflammation, treated HCC, and produced better survival outcomes than Lenvatinib, an FDA-approved HCC drug, in an animal model.

The researchers noted that miR-22 decreased activity for several genes, including Gal1. They decided to explore whether decreasing Gal1 could be an important mechanism for how miR-22 treats HCC.

To inhibit Gal1, the lab used a short interfering RNA (siRNA), called Igals1. The siRNA was packaged for delivery into adeno-associated virus 9, which prefers to land in the liver. Once in and around the tumor, Igals1 effectively silenced Gal1 in both the cancer and stroma, the supporting tissues in and around the tumor.

Silencing Gal1 a potential treatment for liver cancer

"Silencing Gal1 reduced HCC tumors, which are extremely hard to treat," said Wan. "In addition, we found the therapy reduced Gal1 in the stroma at the tumor margin, so it has a big impact on the tumor microenvironment."

A few adeno-associated virus-delivered gene therapies have been approved by the Food and Drug Administration to treat [genetic diseases](#) such as [spinal muscular atrophy](#) and Hemophilia B. However, few researchers have explored using this approach against tumors. The authors believe this study and other work demonstrate the potential of gene therapy for cancer treatments.

While inhibiting Gal1 may be found to benefit human HCC patients, this approach may present other opportunities.

Gal1 is overexpressed in many types of cancer, including breast, colon,

and lung. In addition, the protein begins building up in diseased livers long before HCC develops. As a result, Gal1 inhibition could be considered for HCC prevention.

"Silencing galectin 1 is potentially a groundbreaking strategy in the fight against [liver](#) cancer," said Tahereh Setayesh, first author of the study and a former post-doctoral researcher in Wan's lab. Setayesh is currently at the Cincinnati Children's Hospital Medical Center. "It offers the potential to treat HCC, as well as holding the promise of prevention, providing a path towards transformative therapies."

More information: Tahereh Setayesh et al, Targeting stroma and tumor, silencing galectin 1 treats orthotopic mouse hepatocellular carcinoma, *Acta Pharmaceutica Sinica B* (2023). [DOI: 10.1016/j.apsb.2023.10.010](#)

Provided by UC Davis

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