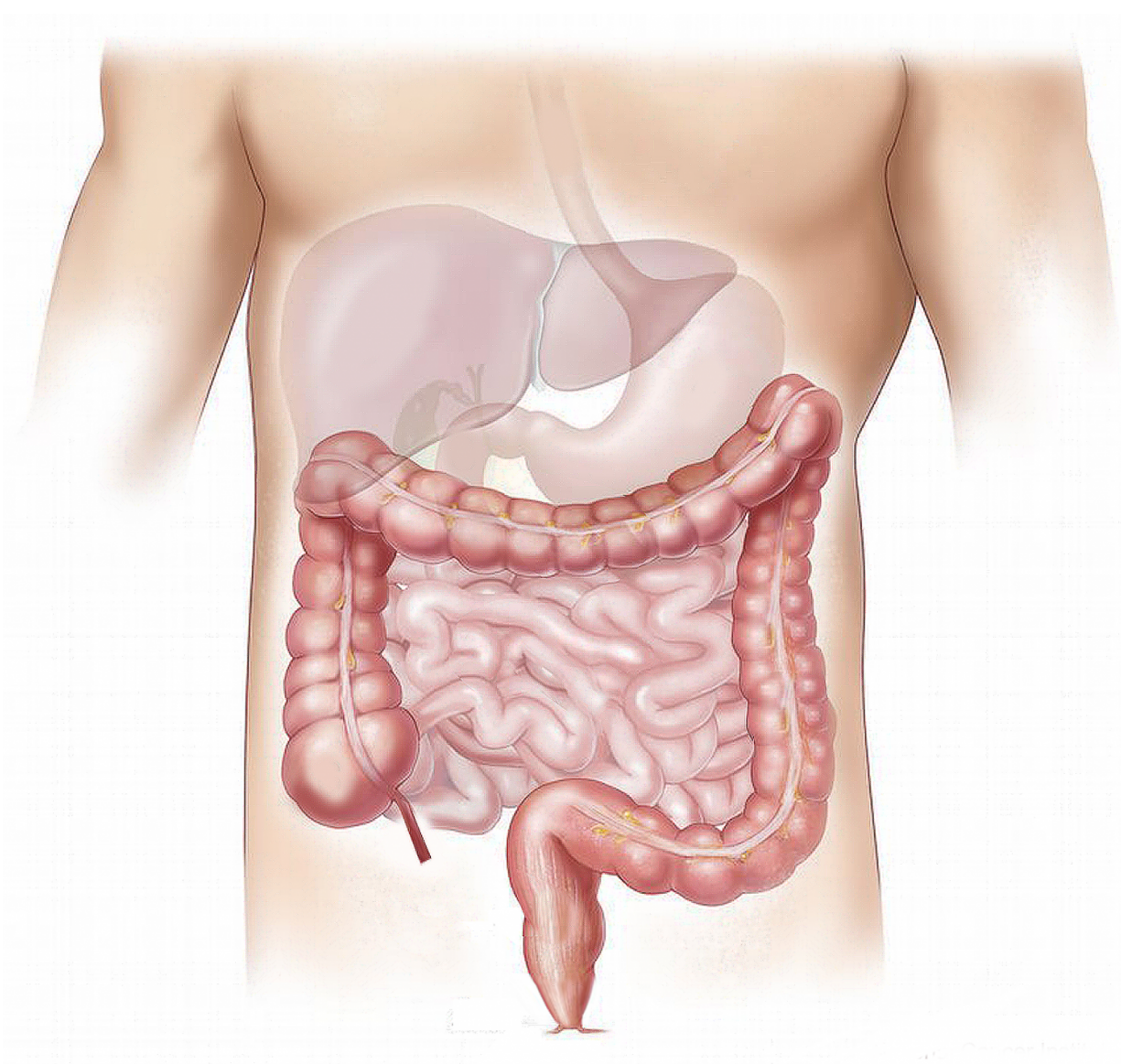


Study identifies miR122 target sites in liver cancer and links a gene to patient survival

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A new study of a molecule that regulates liver-cell metabolism and suppresses liver-cancer development shows that the molecule interacts with thousands of genes in liver cells, and that when levels of the molecule go down, which often happens during liver-cancer development, the activity of certain cancer-promoting genes goes up.

The findings could one day help doctors better predict survival in liver cancer patients and help determine whether the molecule – called microRNA-122 (miR-122) – should be developed as an anticancer drug.

The study, reported in the journal *Molecular Cell*, was led by researchers at The Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC – James) and at Rockefeller University's Howard Hughes Medical Institute.

The researchers sought to biochemically (rather than computationally) define all miR-122 target sites in the liver and hepatocellular carcinoma (HCC), the most common form of liver cancer, and to learn which target [genes](#) were critical for liver cancer development or progression. miR-122 is found almost exclusively in liver cells, where its role includes regulating cholesterol and lipid metabolism.

The researchers identified more than 11,000 miR-122 binding sites in a mouse model. They further found that:

- miR-122 targets nearly 4,800 genes in humans;
- Of these targets, 965 are shared with mice;
- Of the shared targets, a majority are more highly expressed in HCC tumor tissue from patients;

- Loss of miR-122 in HCC results in the over-expression of certain cancer-related genes.

Increased levels of three conserved [target genes](#), BCL9, SLC52A2 and STX6 in tumor tissues could predict poor survival of human HCC patients.

"Our goal is to understand how miR-122 regulates liver metabolism and suppresses cancer development, and to identify common targets in humans and mice that may be involved in HCC development," says co-principal investigator and OSUCCC – James researcher Kalpana Ghoshal, PhD, associate professor of pathology. "That knowledge is critical for determining whether this molecule should be developed as a possible therapeutic agent for liver [cancer](#)."

The findings significantly extend the number of miR-122 binding sites identified by earlier studies because the methods used by the investigators identified sites that other techniques miss, Ghoshal adds. (Note: one gene can have multiple microRNA target sites.)

For this study, Ghoshal and her colleagues used a mouse model that lacked miR-122, along with normal mice; [liver cancer](#) tissues and normal [liver](#) tissues from nine HCC patients; and data from 373 HCC patients in The Cancer Genome Atlas Liver Hepatocellular Carcinoma dataset.

Other key findings include:

- While miR-122 is highly conserved (it's present in [liver cells](#) from fish to humans), a large proportion of miR-122 targets were species specific;
- The findings revealed binding sites that earlier studies missed; the consequences of miR-122 binding to the additional sites need to be determined;

- Human HCC has a core set of conserved miR-122 binding sites.

More information: Joseph M. Luna et al. Argonaute CLIP Defines a Deregulated miR-122-Bound Transcriptome that Correlates with Patient Survival in Human Liver Cancer, *Molecular Cell* (2017). [DOI: 10.1016/j.molcel.2017.06.025](https://doi.org/10.1016/j.molcel.2017.06.025)

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