LAY ABSTRACT

TITLE: Putative Imprinting Control Regions with Aberrant Blood-Based DNA Methylation are Associated with Hepatocellular Carcinoma Risk

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The most common type of liver cancer is hepatocellular carcinoma (HCC), and it is a leading cause of cancer related deaths in the United States. Diagnosing liver cancer early gives patients the best chance at successful treatment. However, HCC is often not found until more advanced stages when symptoms occur. Because the liver is deep inside the body, testing it directly usually requires invasive procedures like biopsies or surgery. Scientists want to use non-invasive blood tests to test for cancer risk early. One test is to look at DNA methylation, or tiny chemical “tags” on our DNA. These tags can happen when we are exposed to pollution and chemicals, or when we have certain diseases. However, tags in our liver cells are not always present in our blood cells. In this study, the researchers wanted to create a blood test that could accurately measure liver health.

STRIVE researchers analyzed the DNA in blood samples from people with and without liver cancer. They found tags that were common in the blood samples from patients with liver cancer. Several of these tags belonged to regions in our DNA called Imprinting Control Regions (ICRs). ICRs are different from most parts of our DNA because chemical tags on ICRs are set very early in life and are the same across different organs. That means that tags on ICRs in our blood cells match the tags on ICRs in our

liver cells. Researchers can therefore look at tags on ICRs from a blood test to see what is happening inside our livers.

The genes (sections of DNA) linked to these ICRs play direct roles in major liver diseases. They are involved in liver inflammation (hepatitis), fat buildup (fatty liver), and rapid cell growth and tumor development (which can become cancer). ICR tags are the same across organs in the body and change when we are exposed to environmental exposures. Finding these tags in blood is an important breakthrough. It opens the door for simple, non-invasive blood tests that could help doctors spot liver cancer risk early and act before cancers develop.