OCR 6901A: A Novel piRNA-based Drug Candidate for Hepatocellular Carcinoma (HCC)

Yale

PIWI-interacting RNAs (piRNAs), a class of small noncoding RNAs, stabilize the genome at transcriptional and post-transcriptional levels. We identified and tested a number of tissue and cancer-type specific piRNAs as potential therapeutic candidates.

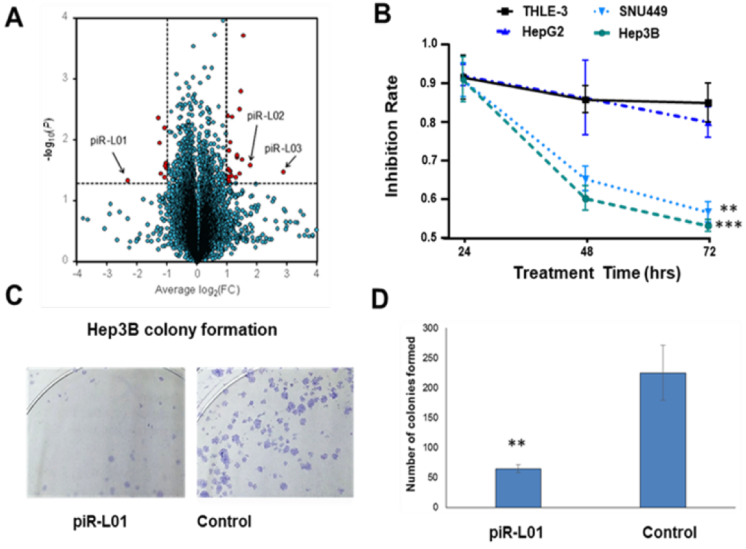

Figure 1. Identification of tumor suppressing piRNAs in HCC. **A.** Underexpressed piRNAs in the HCC tissue identified by array-based piRNA expression profiling. **B.** Restoration of piR-37213-L01 inhibits (>50%) growth of HCC cell lines. **C & D**. 70% reduced colonies formed in piR-37213-L01 treated Hep3B cells.

Lead Innovator: Yong Zhu, Ph.D.
IP status: PCT/US17/19741 (50+ specific piRNA sequences for several cancer types).
References: Fu *et al.* 2015; Jacobs *et al.* 2016, Jacobs *et al.* 2018

We profiled the expression of >23,000 piRNAs in the liver tissue and identified piRNAs that are under- or over-expressed in liver cancer relative to normal liver tissue (red dots in Fig.1A). We have demonstrated anti-cancer effects of down-regulated **piR-37213-L01** both *in vitro* (cell proliferation, and colony formation) (Figure 1) and *in-vivo* (xenograft mouse models in Figure 2). The ***anti-cancer effect of piR-37213-L01*** was ***highly specific for liver*** cancer and had no effect on other cancer types tested (breast, lung, glioma, prostate, etc.). Work invloving testing **piR-37213-L01** in PDX mouse models and uncovering the mehanism of action is under way.

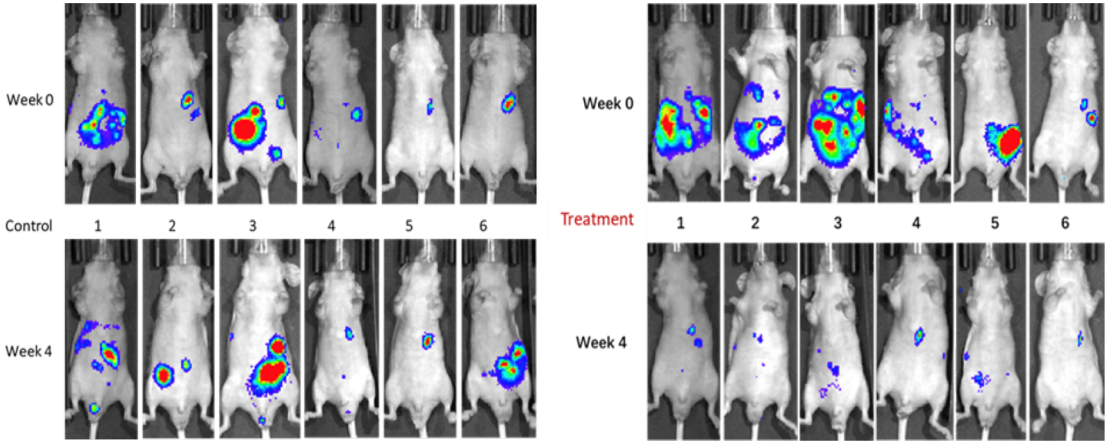

Figure 2. *In vivo* anticancer efficacy of LNP-piR-37213-L01 via systematic delivery. Lipid nanoparticles (LNP) was successfully used to systemically deliver piR-L01 to liver cancer cells via tail vein injection. Mice were treated twice a week for 4 consecutive weeks. Tumor signals are significantly reduced (>90%, P<0.001) after 4-week treatment.

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