235 A Novel piRNA-based Drug Candidate for Hepatocellular Carcinoma (HCC)

Asset Overview

Product Type	Nucleic Acid (Novel piRNA-based Drug Candidate for HCC)
Indication	HCC
Current Stage	Pre-clinical
Target(MoA)	PiR-37213
Brief Description	• Identification and test for tissue and cancer-type specific PIWI-interacting RNAs (piRNAs) • 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 • piR-37213-L01 works in PDX mouse models and uncovering the mechanism of action is under way
Organization	Yale University

Differentiation

□ **Unmet need in HCC**

- According to 2015 statistics from National Cancer Institute, liver cancer is the tenth most common malignant tumors worldwide and accounts for large fraction of overall cancer mortality. The most common type of liver cancer is hepatocellular carcinoma (HCC), which currently lacks effective treatment option

□ **PIWI-interacting RNAs (piRNAs)-mediated epigenetic control of cancer-related processes**

- Roughly 26–31 nucleotides in length and purportedly existing in over 20 000 unique species in the human genome
- piRNAs play a critical role in safeguarding the germ line against transposon-induced insertional mutations
- piRNAs may also have essential functions in the soma, where they have been shown to induce histone modification and DNA methylation in a sequence-specific manner, highlighting the possibility of piRNA-mediated epigenetic control of cancer-related processes in human somatic cancers
- While miRNAs have been implicated in almost every cancer type, virtually nothing is known about the far more abundant piRNAs in the carcinogenic process

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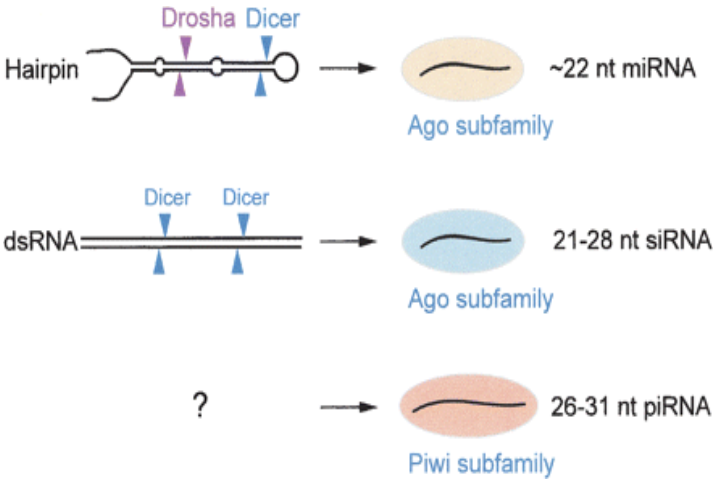
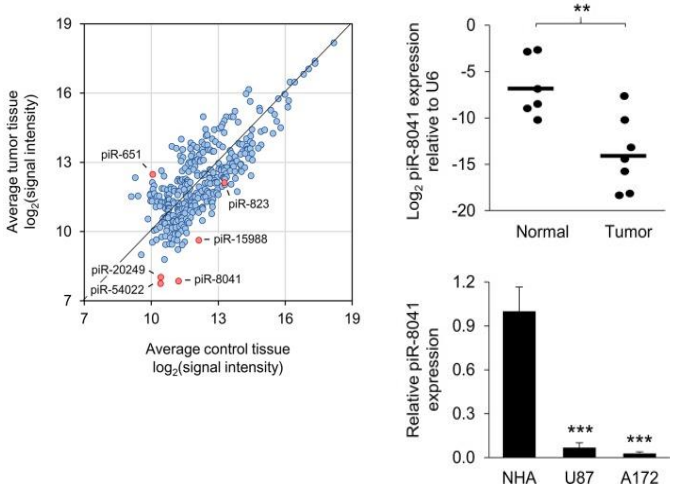
Key Data

Classification of small RNAs

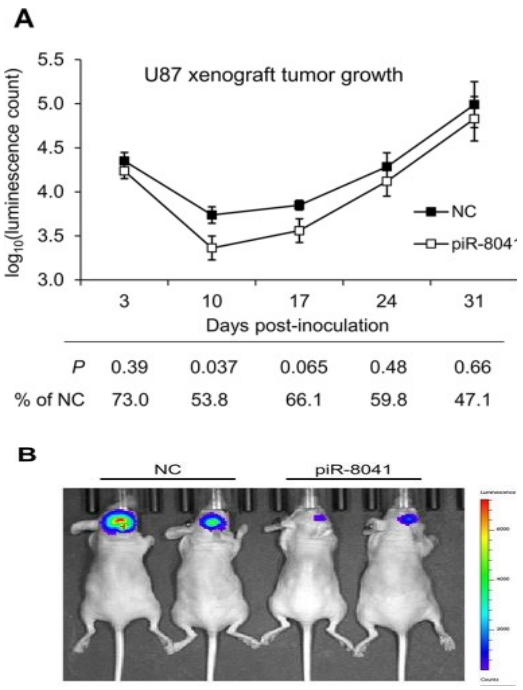


Definition and classification of small RNAs conventionally relies on their biogenesis mechanism. Two relatively well-defined classes of small RNAs include microRNAs (miRNAs) and small interfering RNAs (siRNAs). The biogenesis mechanism for piRNAs is currently unknown.

piR-8041 reduces U87 cell growth in an orthotopic xenograft model



piRNA expression profiling results and confirmation of piR-8041 underexpression in GBM relative to normal brain tissue.



piR-8041 reduces U87 cell growth by nearly 50% 10 days after treatment in an orthotopic xenograft model.

Oncotarget. 2018 Dec 28;9(102):37616-37626. doi: 10.18632/oncotarget.26331

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Fig. 1

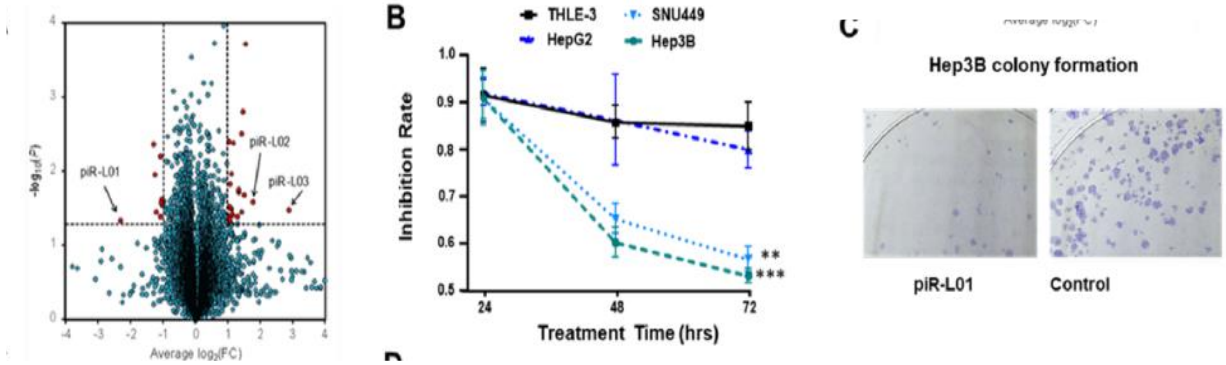

Fig. 2

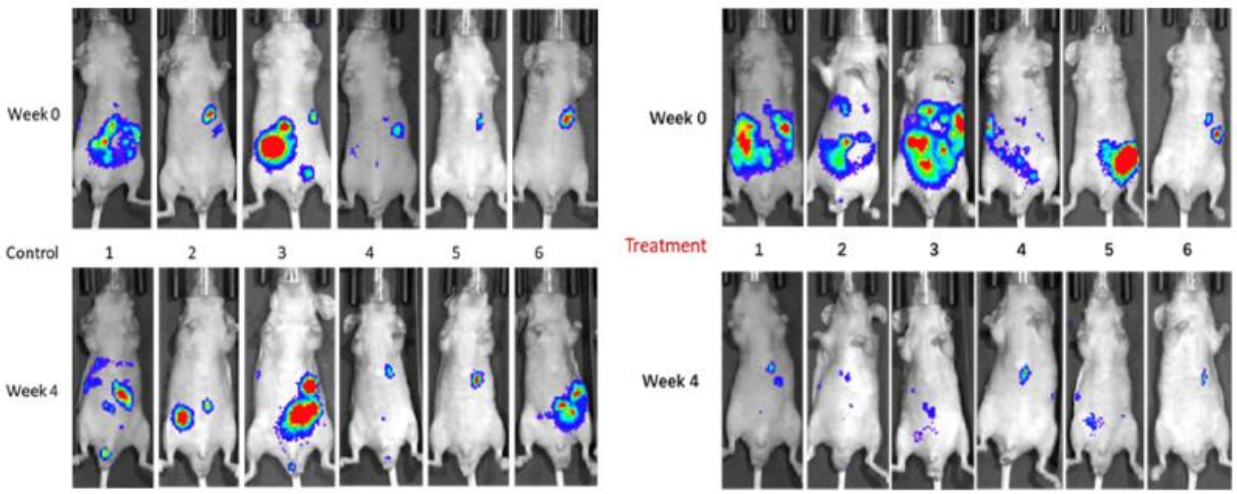

Fig. 1
A. Under-expressed piRNAs in the HCC tissue identified by array-based piRNA expression profiling.
B. Restoration of piR-37213-L01 inhibits (>50%) growth of HCC cell lines.
C & D. 70% reduced
colonies formed in piR-37213-L01 treated Hep3B cells
Fig. 2
Lipid nanoparticles (LNP) was successfully 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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Intellectual Property

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Country	US, EP, JP, CN, AU

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