A New Class of piRNA-based Cancer Therapeutics

OCR Number: OCR 6901

Description:

**PIWI-interacting RNAs (piRNAs)** are a novel class of small noncoding RNAs (24-32 nt), that guide PIWI proteins to transposons and stabilize the genome. piRNA class includes >30,000 unique types with <100 gene targets, functions both in cytoplasm and in nucleus and mediates both transcriptional and post-transcriptional regulation.

Advantages of piRNA-based therapeutic approach compared to siRNA and miRNA-based approaches:

- **higher target specificity**, due to longer seed sequences of piRNAs.
- **higher tissue specificity**, as many PIWI proteins are expressed only in tumor cells.
- **gene-specific DNA methylation** and gene silencing at transcriptional level
- **higher efficacy and lower toxicity**.

- Demonstrated cancer-specific in-vitro and in-vivo efficacy in several cancer models, including liver cancer and glioblastoma. Potential diagnostic and research tool applications.

- **Lead Innovator**: Yong Zhu, Ph.D.

- **IP status**: PCT/US17/19741 filed.

- **References**: Oncotarget (in press); CEBP (2016); Carcinogenesis (2015).

![Graph showing U87 xenograft tumor growth](image)

<table>
<thead>
<tr>
<th>Days post-inoculation</th>
<th>% of NC</th>
<th>pIR-8041</th>
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<tbody>
<tr>
<td>3</td>
<td>73.0</td>
<td>53.6</td>
</tr>
<tr>
<td>10</td>
<td>66.1</td>
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<tr>
<td>17</td>
<td>69.6</td>
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<td>24</td>
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<tr>
<td>31</td>
<td>80.8</td>
<td>44.1</td>
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</tbody>
</table>

![Figure](image)

*Figure, pIR-8041 reduces cell growth by ~50%.*

Top: Bioluminescence measurements of luciferase-expressing intracranial tumors at multiple time points. Bottom: Images of representative mice from each treatment group on day 10 after tumor implantation.

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