



NIH Awards Three Grants Supporting RNAi, microRNA Rx Development

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The National Institutes of Health last month earmarked nearly \$650,000 to fund three research projects focused on developing RNAi- and microRNA-based therapeutics for cancer and Huntington's disease.

The first grant was awarded to Mirna Therapeutics to support the company's work on creating therapeutic miRNA mimics as cancer treatments.

The company has "identified approximately ten tumor suppressor miRNAs and is in the process of developing mimetics for two of these that will be subjected to efficacy and safety studies using advanced rodent and primate studies," Mirna said in the grant's abstract.

With the NIH's grant funding, which is worth \$287,270 and is set to run from July 1 until the end of March 2011, Mirna plans to develop "nucleotide analogs to improve the stabilities and activities of mimetics of two miRNAs that have proven to have therapeutic activities in mouse models of several different cancers."

Mirna did not specify in the abstract the two miRNAs that are the focus of the NIH-funded effort. The company has, however, disclosed that it is working on mimics for miR-34a as a therapy for prostate and other solid tumors and an undisclosed miRNA for solid tumors including non-small cell lung cancer. Mirna has said that it expects to file investigational new drug applications for the two agents by 2011 ([GSN 6/24/2010](#)).

This month, Mirna announced the publication of [data](#) in *Cancer Research* showing that a miR-34a mimic, formulated with proprietary lipid-based nanoparticles, reduced the expression of "multiple" targets of the miRNA when systemically delivered to two different mouse models of non-small cell lung cancer.

Further, treatment induced apoptosis and inhibited the growth of established tumors, but

did not trigger changes in serum levels of cytokines or liver and kidney enzymes, Mirna said.

In the grant's abstract, the company said it hopes to develop mimics that are up to ten times more effective than the molecules it has used in efficacy studies to date. These mimics will be "coupled with delivery agents" developed in parallel, and the combinations will be tested in mouse models.

The second grant was awarded to Sirnaomics to support development of a multi-targeted siRNA-based treatment for glioblastoma multiforme.

"Despite decades of intensive surgical treatment, chemotherapy, radiotherapy, and tremendous basic science and clinical research focused on combating this disease, the prognosis [for the disease] remains virtually unchanged, with survival rates still measured in months," the company said in the grant's abstract. Yet research has identified a number of intracellular molecules and their associated signaling pathways as potential therapeutic targets for the disease.

In line with its strategy of developing therapies containing multiple siRNAs, Sirnaomics said in the abstract that it will create three cocktails: one containing siRNAs against epidermal growth factor receptor, vascular endothelial growth factor, and O6-methylguanine-DNA-methyltransferase; one with siRNAs against EGFR, VEGF, and matrix metalloproteinase 9; and one with siRNAs for EGFR, VEGF, and transforming growth factor.

Each will be packaged in polymer and liposomal nanoparticles, and their efficacy will be tested in human and mouse glioma cell line tumor models, and the delivery systems will be evaluated and optimized for the most effective siRNA cocktail, Sirnaomics said.

The company added that it will examine the cocktails in combination with the chemotherapeutics temozolomide and bevacizumab.

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