



Office of Technology  
Development  
800 Huntington Avenue  
Boston, Massachusetts 02115  
[www.idi.harvard.edu](http://www.idi.harvard.edu)

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**CELL-TYPE SPECIFIC SYSTEMIC  
DELIVERY OF siRNA**

**Key Words:** RNAi, siRNA, cell-type specific, systemic delivery, therapeutics, reagents.

**Application:** Delivery of small interfering siRNAs to specific cell types for human therapeutics. Self-delivering reagents as a more effective alternative to electroporation, chemical, lipid or polymer-based transfection methods.

**Inventor(s):** Judy Lieberman, M.D., Ph.D. and Erwei Song, Ph.D.

**Invention Summary:**

The effectiveness of gene silencing using RNAi is dependent on efficient delivery of siRNAs into cells. This delivery method allows specific disease causing genes to be turned off by siRNAs that enter only specific cells in both *in vitro* and *in vivo* settings, thereby avoiding potential side effects of delivery into non-targeted cells. Through cell specific systemic delivery of siRNAs, we have taken a significant step towards using siRNAs as human therapeutics.

This delivery method utilizes a cell-targeting moiety that binds to a specific molecule on a target cell such as a cell-surface receptor or surface antigen and an RNA interference-binding moiety that binds to the siRNA of interest. Experiments have shown that this delivery method selectively delivers the siRNA only into the cells expressing a specific surface receptors or antigen. The efficacy has been demonstrated *in vivo* using both subcutaneous and intravenous administration. In one experiment, the tagged siRNAs were absorbed only by mouse melanoma cells engineered to carry a specific receptor and not by normal melanoma cells. Also, siRNAs designed to shut down known cancer-causing genes were injected into mice implanted with engineered melanoma cells. Results after nine days showed that the tumors were about half the weight of tumors in the control group.

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PCT Application # PCT/US2005/029111, Publication # 2006/023491  
Japanese Application # 2007-527944, Publication # 2008-509705

**Availability:** Nonexclusive worldwide licenses for therapeutics and research reagents.

**Contact:** Ryan Dietz  
Director, Office of Technology Development  
617-278-3463 dietz@idi.harvard.edu

