
Small Business Evaluation and Entrepreneur's (SBEE) Program

A collaboration between the NU Nanoscale Science and Engineering Center NSEC and

Kellogg Graduate School of Management

Directors: Professors Barry Merkin and Chad A. Mirkin

PROPOSAL

The purpose of the new Small Business Evaluation and Entrepreneurs (SBEE) Program is to facilitate the commercialization of new technological developments, by providing scientists with the tools to successfully launch new businesses. Through this program scientists propose ideas for starting businesses to a team of Kellogg students. Students select proposals and provide research and write business plans for presentation to investors. Your completed proposal will be forwarded for review to Kellogg students for inclusion in the SBEE Program. Please be advised that limited time and resources make acceptance of all projects submitted impossible. However, projects will be solicited throughout the year.

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Names Erik Sontheimer and Richard Carthew

Collaborators _____

Department(s) Biochemistry, Molecular Biology & Cell Biology

Primary Tel 847/467-6880 (E.S.) Primary Email erik@northwestern.edu

Title of Project:

Silentech, Inc.: Improving RNA Interference for Therapeutics

Summary:

One of the most exciting advances in recent years has been the discovery and characterization of RNA interference (RNAi) to silence genes, and the use of short interfering RNA (siRNA) to trigger this mechanism. By creating short RNA sequences complementary to specific genes, one can selectively inactivate those genes. This suggests the possibility of using RNAi to treat virtually any disease that involves aberrant gene expression. Many recent developments underscore the great potential of RNAi, but two are particularly noteworthy: (i) the 2006 Nobel Prize in Medicine was awarded to the discoverers of this phenomenon; and (ii) Sirna Therapeutics, one of the leading companies in this arena (founded in 2001), was recently acquired by Merck for \$1.1 billion.

In spite of the recognized potential of RNAi, however, practical hurdles do exist, and the mechanism is never %100 effective in silencing genes. The processes that modulate this inhibition of RNAi are incompletely understood, but at least one of the naturally occurring pathways involves enzymes that degrade siRNA within cells. Several efforts are underway to counteract the phenomenon. Most of the approaches attempt to improve efficiency by chemically modifying the nucleic acids to increase their survival.

INTERNATIONAL INSTITUTE FOR NANOTECHNOLOGY (IIN)

2145 Sheridan Road, Evanston, IL 60208

Tel: (847) 467-4228 Email: nanotechnology@northwestern.edu

Silentech takes a novel approach to enhancing RNAi efficacy by blocking the mechanisms that inhibit RNAi. The founders have developed a unique method to discover RNAi inhibitors and have demonstrated that the addition of siRNAs against these inhibitors significantly blocks the inhibition of RNAi in cells. The result is an increased effectiveness of the RNAi mechanism itself, by blocking the inhibitor, independent of the specific gene that is chosen to be silenced. By analogy with conventional vaccines, we call these siRNA/small molecules against the inhibitors adjuvants, because of their ability to enhance the RNAi process.

The implications of using adjuvants to increase RNAi efficacy are manifold. First, it does not require manipulation of the targeting siRNA, which reduces time, cost, and complexity. Second, because it modulates the mechanism rather than the targeting siRNAs, it can have broader applicability rather than requiring customization for each target. Third, it in essence can improve the sensitivity of detection of an effect because of more complete silencing. This suggests that less targeting siRNA would be required for the same efficacy, which could obviate the need to use multiple siRNAs, or fewer of them, which in turn could reduce user costs and reduce the risk of unwanted side-effects.

Potential Applications:

Silentech's mission is to use this unique method to systematically identify RNAi inhibitors, and then develop and characterize siRNA adjuvants that block these inhibitors for commercial use. We will concentrate on developing the adjuvants, and outsource the manufacturing, marketing, and sales. The company has the exclusive world-wide rights to the technology and the use of adjuvants, as well as to the intellectual property rights to the adjuvants developed. As new adjuvants are identified and characterized they, too, will be patented.

Silentech plans to sell these adjuvants to academic and commercial research laboratories as our initial target market to generate revenue. They would make useful aids for studying functional genomics. This market can be approached quickly because, as a laboratory tool without clinical application, the products would not be subject to regulatory approval. We will reinvest these revenues into the business for the R&D to generate, protect, and optimize more adjuvants.

The greater potential, however, is in a second arena: therapeutic applications. RNAi technology in general, and siRNA agents in particular, are aggressively being developed for the treatment of numerous diseases. Already such agents are in clinical trials.

Just as the use of adjuvants can potentiate the immune response to many vaccines, we believe that the use of our adjuvants to block RNAi inhibition in RNAi-based therapies could improve the efficacy of these agents as well. It would allow the use of less siRNA to achieve the desired response, which could reduce off-target side-effects, as well as reduce risks of potential toxicity that siRNA might cause.

We will look to target one or a few appropriate diseases that appear amenable to treatment by RNAi therapy, and undertake the preclinical work to serve as the basis for finding strategic alliances to develop the therapeutic compound. We intend to do much of this work through co-development as an approach.

There is additionally a third sector that can be addressed by the adjuvant technology, namely the agricultural/agbio area. The continued development of genetically modified crops and livestock to feed the world's population, and the increasing interest in improving biofuels production make these areas ripe for our offerings. This, however, is not an area of emphasis at this time, and will only be considered opportunistically, in the form of collaborations and alliances.