

Molecular & Cellular Imaging: From the Bench to the Bed

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Highlights

- Epigenetic modification using RNA interference is a potential powerful therapeutic tool
- Delivery of oligonucleotides in vivo is hampered by their fast degradation and elimination from the bloodstream
- Theranostic probes are designed to deliver siRNA therapies to the site of pathology and to monitor this delivery non-invasively

Title: “Theranostic Probes for siRNA and microRNA Therapies”

Targeted audience: This presentation is intended for graduate students, postdoctoral scientists, and physicians (radiologists) who are either new to the field of Molecular and Cellular Imaging or wish to be updated on the current state-of-the-art in its applications to various human pathologies.

Objectives:

Molecular imaging probes could be used not only for the detection of pathology but also for delivery of therapy and for monitoring of this delivery. Termed “theranostic probes”, in many cases they allow for targeted delivery of therapeutics efficiently decreasing the injected dose and reducing systemic toxicity. Furthermore, theranostic probes enable the delivery of therapies that could not be delivered in their native state due to their fast degradation in the bloodstream. This presentation will focus on delivery of oligonucleotides for siRNA and microRNA therapies.

Silencing genes responsible for various pathologies is done using RNA interference mechanism, an innate cellular mechanism for post-transcriptional regulation of gene expression in which double-stranded ribonucleic acid inhibits the expression of genes with complementary nucleotide sequences. Its potential as a therapy tool is indisputable, considering that one can use this mechanism to silence virtually any gene with single-nucleotide specificity. Major obstacles in applying RNA interference in vivo are presented by the short circulation half-life of the siRNA molecule, its vulnerability to degradation by nucleases (elimination half-life 2-6 min), and the need to translocate the siRNA into the cytosol, where the RNA interference process takes place.

An essential element in the development and optimization of a siRNA delivery method is the ability to measure the bioavailability and functionality of the siRNA molecule after administration into the body. Noninvasive imaging provides the necessary set of tools to accomplish this in authentic physiologic environments and across time. To facilitate siRNA delivery to tumors and enable in vivo imaging of the delivery, theranostic nanoparticle probes, which allowed for visualization by magnetic resonance imaging/multimodal imaging have been employed.

MicroRNA are a class of post-transcriptional regulators that have been implicated in various cell functions including metastatic potential. Several microRNAs that mediate the process of tumor cell migration and tissue invasion have been identified. This presentation will focus on the study describing targeting miR-10b implicated in breast cancer metastasis using magnetic nanoparticles decorated with locked nucleic acid oligonucleotides as a therapeutic moiety. These nanoparticles have an inherent capacity for noninvasive imaging and obtaining semi-quantitative information about nanoparticle bioavailability in target tissues. This information could be invaluable in a clinical setting for determining the need for re-treatment on a patient-by-patient basis, opening up the possibility for designing individualized therapeutic regimens.

Composition of various theranostic nanoparticles both targeted and non-targeted used for gene silencing will be discussed. Examples of their use in various pathologies in pre-clinical models and in clinic will be presented. Future application of this class of molecular imaging probes will be evaluated in conjunction with conventional therapies. Limitations of these probes for in vivo applications will be highlighted.