RNAi - Technologies, Markets and Companies

Description:

RNA interference (RNAi) or gene silencing involves the use of double stranded RNA (dsRNA). Once inside the cell, this material is processed into short 21-23 nucleotide RNAs termed siRNAs that are used in a sequence-specific manner to recognize and destroy complementary RNA. The report compares RNAi with other antisense approaches using oligonucleotides, aptamers, ribozymes, peptide nucleic acid and locked nucleic acid.

Various RNAi technologies are described, along with design and methods of manufacture of siRNA reagents. These include chemical synthesis by in vitro transcription and use of plasmid or viral vectors. Other approaches to RNAi include DNA-directed RNAi (ddRNAi) that is used to produce dsRNA inside the cell, which is cleaved into siRNA by the action of Dicer, a specific type of RNAse III. MicroRNAs are derived by processing of short hairpins that can inhibit the mRNAs. Expressed interfering RNA (eiRNA) is used to express dsRNA intracellularly from DNA plasmids.

Delivery of therapeutics to the target tissues is an important consideration. siRNAs can be delivered to cells in culture by electroporation or by transfection using plasmid or viral vectors. In vivo delivery of siRNAs can be carried out by injection into tissues or blood vessels or use of synthetic and viral vectors.

Because of its ability to silence any gene once the sequence is known, RNAi has been adopted as the research tool to discriminate gene function. After the genome of an organism is sequenced, RNAi can be designed to target every gene in the genome and target for specific phenotypes. Several methods of gene expression analysis are available and there is still need for sensitive methods of detection of gene expression as a baseline and measurement after gene silencing. RNAi microarray has been devised and can be tailored to meet the needs for high throughput screens for identifying appropriate RNAi probes. RNAi is an important method for analyzing gene function and identifying new drug targets that uses double-stranded RNA to knock down or silence specific genes. With the advent of vector-mediated siRNA delivery methods it is now possible to make transgenic animals that can silence gene expression stably. These technologies point to the usefulness of RNAi for drug discovery.

RNAi can be rationally designed to block the expression of any target gene, including genes for which traditional small molecule inhibitors cannot be found. Areas of therapeutic applications include virus infections, cancer, genetic disorders and neurological diseases. Research at academic centers that is relevant to RNAi-based therapeutics is mentioned.

Regulatory, safety and patent issues are discussed. Side effects can result from unintended interaction between an siRNA compound and an unrelated host gene. If RNAi compounds are designed poorly, there is an increased chance for non-specific interaction with host genes that may cause adverse effects in the host. However, there are no major safety concerns and regulations are in preliminary stages as the clinical trials are still ongoing and there are no marketed products. Many of the patents are still pending.

The markets for RNAi are difficult to define as no RNAi-based product is approved yet but several are in clinical trials. The major use of RNAi reagents is in research but it partially overlaps that of drug discovery and therapeutic development. Various markets relevant to RNAi are analyzed from 2012 to 2022. Markets are also analyzed according to technologies and use of siRNAs, miRNAs, etc.

Profiles of 161 companies involved in developing RNAi technologies are presented along with 229 collaborations. They are a mix of companies that supply reagents and technologies (nearly half of all) and companies that use the technologies for drug discovery. Out of these, 33 are developing RNAi-based therapeutics and 34 are involved in microRNAs. The bibliography contains selected 600 publications that are cited in the report. The text is supplemented with 34 tables and 11 figures.

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