**Exosomes can make the use of circulating miRNA as a biomarker more feasible**

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Abstract  
Circulating miRNAs have also been propos Exosomes can make the use of circulating miRNA as a biomarker more feasible. The aim of gene therapy should be to learn everything there is to know about miRNA activity. ed as potential disease biomarkers. It is critical for precision medicine to provide a system that allows for the rapid verification and confirmation of promising biomarkers based on circulating miRNAs. Concentrating on specific modes of transport (exosomes), fine-tuning sampling and extraction processes, and absolute quantification without using housekeeping gene(s) could allow the use of circulating miRNAs as biomarkers more realistic in the future. You should know which human biological fluid is better for determining the amount of circulating miRNA expression, as well as which pathology this biological fluid is best for. To validate the existence of new circulating miRNAs, separate experiments may be performed. Using a panel of two or more intentionally chosen circulating miRNAs with one or more pathologies, such as tumors, will be more accurate and precise.

The discovery of additional miRNAs linked to disease pathogenesis may help in the creation of hybrid therapies that incorporate miRNA expression control with clinical use. When it comes to miRNAs' potential side effects in clinical trials, caution is advised, with a focus on drug efficacy, tolerability, and viability. To prevent any disruption in the natural regeneration process, the optimum dosage and timing of clinical action with different inhibitors or mimicry of miRNAs should be carefully assessed. Such therapy should be focused on a comprehensive understanding of miRNA actions, including its effects on cellular viability, proliferation, and differentiation. It's also crucial to know how often real miRNAs are expressed. To prevent secondary non-specific side effects, a small decrease or increase in miRNA expression could be the safest alternative.  
MicroRNAs (miRNAs) have the ability to be used as medicinal instruments.  
Since they are needed for multiple cellular homeostasis functions, MiRNAs play a role in a number of disease manifestations outside of tumors, such as cardiovascular disease. However, when it comes to using miRNAs as therapeutics, there are two main approaches: (1) restoring the miRNA target that has been downregulated, or (2) inhibiting the miRNA target that has been overexpressed. 51. MiRNA mimics, which are synthetic double-stranded RNA molecules with an identical sequence to natural miRNAs that can insert into the RISC and replace the missing miRNA 53, can be used to restore the downregulated miRNA target. MiR-34 mimics have been shown to be effective antitumor therapeutics in a number of preclinical studies. MiR-34 mimics encapsulated in lipid nanoparticles, for example, have shown to be effective against liver and lung cancer in vivo. 54 and 55. Bejerano et al. discovered a new therapeutic strategy for regulating macrophage phenotype by delivering miR-21 mimics through nanoparticles, which could be used to prevent post-myocardial infarction remodeling and cardiac failure. Anti-miRNAs, which are oligonucleotides with complementary miRNA sequences, can block the activity of various miRNAs as well as the anti-miRNAs' inhibitory effect on tumor cell growth and inflammation. The 57th. Yang et al. used biodegradable poly (ester amine) and hyaluronic acid shielding (PEA/anti-miR-155/HA–peptide complexes) to create a tumor-targeting anti-miR-155 delivery system for lung cancer therapy. Anti-miR-155 was delivered to lung cancer cells by the PEA/anti-miR-155/HA–peptide complexes, which inhibited tumor growth 58.  
Owing to a range of disadvantages, such as increased blood degradation and the lack of an appropriate dissemination vector, anti-miRs and miRNA mimics have been difficult to use as therapeutic agents in vivo. As a result, synthetic cationic materials including liposomes, polyethylenimine (PEI), and other non-viral polymers that have been used to study the delivery capabilities of miRNA 54,55,56, 58 can now be used as effective gene delivery vectors. Although further research is needed to assess the long-term efficacy and safety of miRNA mimics and anti-miRNAs, these results suggest that systematic delivery of miRNA mimics and anti-miRNAs will solve the challenges of viral-based miRNA delivery, paving the way for miRNA replacement therapy to rapidly reach the clinic.  
The number of oncogenes or tumor suppressors that a specific miRNA is targeted at, which describes the number of oncogenes or tumor suppressors that a specific miRNA is aimed at, is unclear. The ability of microRNAs to target several genes is appealing because it may allow for the targeting of multiple compensatory pathways 60. However, since a single miRNA target can contain both oncogenes and tumor suppressors, as well as a number of non-oncogenic targets, designing selective miRNA-based therapy is more complicated 61. Furthermore, they could have controlled genes involved in normal cell homeostasis that we don't know about by decreasing or increasing the level of target miRNA expression, particularly at non-physiological concentrations, which may have negative consequences. 62  
Drug resistance to chemotherapy in cancer patients continues to be a problem that is obstructing emerging treatment practices in clinical practice. Several studies have shown that altering the expression of specific miRNAs can affect chemotherapeutic drug sensitivity or that miRNAs are biologically involved in the body's resistance response 63, 64. Deregulated miRNAs are compared to many standard glioma treatments, including temozolomide and demethoxycurcumin, which can modulate chemotherapeutic drug resistance 65, 66. Data suggests that such miRNAs could be useful in the treatment of malignant gliomas, such as glioblastoma multiforme (GBM), which is particularly resistant to chemotherapy 66. According to increasing proof, MiRNAs 67, 68 regulate the ATP-binding cassette (ABC) transporter family of proteins that activate drug resistance. Lv et al. discovered that miR-155 is commonly expressed in doxorubicin-resistant non-small-cell lung carcinoma (NSCLC) cells and that inhibiting miR-155 with antisense oligonucleotides reversed doxorubicin resistance and lowered the ABC transporters breast cancer resistance protein (BCRP), P-glycoprotein, and multidrug resistance-associated proteins in the doxorubicin-resistant cell line NSCLC. The pathways controlled by miRNAs in the resistance to chemotherapeutic drugs are also being investigated. In certain cases, co-administration of conventional chemotherapeutic drugs with the selected miRNA (miRNA mimic or anti-miRNA) may help mitigate drug resistance by blocking key genes that contribute directly to the drug's poor bioavailability or by alternate signaling mechanisms, such as miR-155 for lung cancer. Nanomedicine has elegantly attempted to cure multiple gene polymorphisms and mutations in complex diseases 177-191 using gene therapy techniques 165-176.

Final thoughts

Circulating miRNAs are also thought to be possible disease biomarkers. The availability of a method that allows for the rapid verification and validation of promising biomarkers based on circulating miRNAs is crucial for their advancement in personalized medicine. Concentrating on particular modes of transport (exosomes), refining sampling and extraction methods, and total quantification without the use of housekeeping gene(s) could help make the use of circulating miRNAs as biomarkers more practical in the future. You should know which biological fluid from the human body is better for measuring the volume of circulating miRNAs expression, as well as which pathology this biological fluid is best for. Independent tests can also be carried out to confirm the presence of new circulating miRNAs. It would be more reliable and precise to use a panel of two or more deliberately selected circulating miRNAs with one or more pathologies, such as tumors.

The identification of additional miRNAs linked to disease pathogenesis may aid the development of hybrid therapies that combine miRNA expression regulation with clinical application. When it comes to possible adverse effects of miRNAs in clinical trials, caution should be exercised, with an emphasis on drug safety, tolerability, and feasibility. The optimal dosage and pacing of therapeutic action with specific inhibitors or mimicry of miRNAs should be carefully measured to avoid any disruptive interruption in the natural regeneration process. A detailed understanding of miRNA behavior, including its effect on cellular viability, proliferation, and differentiation, should be the subject of such therapy. Understanding the extent of expression of specific miRNAs is also important. A slight decrease or rise in miRNA expression may be the best choice for preventing secondary non-specific side effects.

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