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The Role of Microrna (Mirna)S in Cancer Diagnosis and Therapy

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MiRNAs are non-coding single-stranded RNAs comprised of 20-22 nucleotides and considered as a novel class of gene regulators. It has been suggested that miRNA expression correlates with classification of various cancers. About half of the annotated human miRNAs are located in fragile sites of the genome suggesting that these small molecules might have a vital function in cancer progression. miRNAs can regulate gene expression transcriptionally or translationally. There is an emerging evidence that miRNAs are involved in cancer pathogenesis. A number of studies have detected frequent alterations of miRNA expression in a variety of human malignancies including prostate cancer. We have recently demonstrated a widespread deregulation of miRNA expression in human prostate cancer. The status of the selected miRNAs, in human prostate cancer cell lines DU-145, LNCaP, LAPC4, PC3 and prostate cancer specimens have been analyzed. We have transfected these cell lines with precursor miR- and anti miR- molecules and compared the gene expression profiles. We have also compared the targets for these selected miRNAs identified biologically in prostate cancer cells and in three different databases. The expression status of selecttargets have been verified and the biological effects of these targets on prostate cancer cell lines are studied. The results obtained in these studies demonstrate that microRNA(s) can be used to find new markers for prostate cancer progression and to define promising targets for prostate cancer therapy.

From chemotherapy and radiotherapy to molecular targeted therapy, in recent decades, we have witnessed the acceleration of cancer treatments. However, nowadays, it has encountered obstacles due to multi-drug resistance, drug-induced toxicity and the insufficient disruption of cancer pathways. Thus, it is required to have more efficient approaches for cancer treatments. MicroRNAs (miRNAs) are perhaps the most researched genes in the last decade. They have been reported to play significant roles in cancers and are considered to be applied in targeted cancer therapies. Here, we will firstly review the implications of miRNAs in clinical use from the aspects of miRNA biogenesis and biological functions, followed by the diagnostic and prognostic values of miRNAs. Furthermore, the application of miRNAs in pre-clinical cancer models and clinical trials regarding miRNAs will also be discussed. Moreover, since miRNA delivery is the biggest challenge for miRNA based therapy, the commonly used delivery methods will then be reviewed. The miRNA combinational therapy with chemotherapy, radiotherapy, molecular targeted therapy and immunotherapy will be reviewed and discussed at last.

Over the last 10 years a small RNA revolution has swept biology. In 1998 interference RNA (RNAi) was discovered as an experimental tool by Andy Fire and Craig Mello, a finding that was awarded with the 2006 Nobel Prize for Physiology or Medicine. Although the biology of RNAi is still not understood, it has become a powerful experimental tool and is currently being developed for human gene therapy. During a similar timeframe and linked in some aspects to RNAi, microRNAs (miRNAs) were discovered as a new class of regulatory RNAs in animals, plants and viruses. miRNAs are transcribed from endogenous genes as long, primary RNA transcripts and are processed to their mature form: a single-stranded RNA with a length of approximately 22 nucleotides, indistinguishable from a small-interfering RNA (siRNA), the mediator of RNAi. In animals these long RNA precursors (pri-miRNAs) are processed in the nucleus by the RNase III enzyme Drosha and Pasha/DGCR8 to form the approximately 70-base pre-miRNAs . Pre-miRNAs are exported from the nucleus by Exportin-5, processed by the RNase III enzyme Dicer and incorporated into an Argonaute-containing silencing complex (RISC). miRNAs are thought to regulate gene expression post-transcriptionally by forming Watson-Crick base pairs with target mRNAs. Their mechanism of action is still under debate, but likely includes inhibition of translation and mRNA degradation. In animals, most miRNAs are thought to form imperfect base pairs with their target mRNA(s) and these interaction sites are enriched in 3′ un-translated regions (3′-UTRs). As a consequence, miRNA target identification using computational approaches is non-trivial.The public database for miRNAs, miRBase release 9.1, currently lists 474 human microRNAs and estimates for the total number of human microRNAs range from over one thousand to tens of thousands. Although miRNAs have only been studied intensely for the last 5 years, important functions for miRNAs in animal development and, potentially, human disease, have already emerged.