Preface: MicroRNAs as Novel Cancer Biomarkers and Therapeutic Targets

MicroRNAs (miRNAs) are endogenous small non-coding RNA molecules shown to have a key role in the regulation of gene expression. MiRNAs appear dysregulated in a wide variety of human tumors and their possible direct involvement in the pathogenesis of cancer has been proposed. In addition, the expression of selected miRNAs was found to correlate with clinicopathological features of aggressiveness and to be able to predict patients’ clinical outcome and/or response to treatment. Such findings, together with the evidence that miRNAs are highly stable in formalin-fixed tissues and can be directly measured in body fluids, have highlighted their potential as diagnostic or prognostic/predictive biomarkers. Moreover, the role of miRNAs functioning as oncopgenes and tumor suppressors in specific cell contexts has generated great interest in their possible use as novel targets or tools for anticancer therapies. This special issue by experienced contributors provides an up-to-date overview of miRNA-based investigations in the field of oncology.

The more relevant aspects concerning miRNA expression evaluation in tumors are addressed by Dr. De Cecco and colleagues. They discuss the different steps of the miRNA analysis processes (including preanalytical aspects, available analytic tools for miRNA profiling, and as postanalytical strategies), which have substantial impact not only on the biological interpretation of data and their translational application, but also on the possibility to compare results from different studies and explain controversial data generated thus far.

Dr. Fendler and Dr. Jung make an extensive survey of the potential of miRNAs as novel diagnostic and prognostic markers in urological tumors, with special reference to miRNAs detectable in patients’ blood and urine, in view of the possible development of noninvasive systems for disease detection and monitoring. Although a certain number of miRNAs appear to fulfill the criteria for being possible novel biomarkers in such diseases, none of them can be translated into the clinical setting due to the lack of independent validation in large patient cohorts and prospective studies.

Dr. Mauger-Sacca and colleagues focus their contribution on miRNAs that have been demonstrated to play a crucial role in the pathobiology of prostate cancer, through their connection with multiple tumor-promoting activities, as well as on the possibility to exploit them as novel therapeutic targets or tools. In fact, a handful of miRNAs have been successfully modulated by the use of precursors and inhibitors in animal models of prostate cancer, thus providing the proof of principle of the possibility to develop miRNA-based strategies for the treatment of the disease, although major issues, such as delivery strategies and toxicology, need to be improved.

A large body of evidence indicates that aberrant miRNA expression is implicated in the anticancer drug resistance phenotype. In their review, Dr. Maftouh and colleagues focus on the molecular mechanisms by which specific miRNAs can contribute to resistance of non–small cell lung cancer to epidermal growth factor receptor–targeted agents and discuss the possibility to modulate their expression to increase tumor cell chemosensitivity.

Besides miRNAs themselves, single nucleotide polymorphisms (SNPs) within miRNA binding sites represent a novel kind of cancer biomarkers. Drs. Preskill and Weidhaas make a review on functional SNPs within miRNA binding sites for which a potential as cancer biomarkers has been reported. Although most of the available information available so far is related to the association with cancer risk, an increasing number of studies demonstrate the potential of these SNPs as novel prognosticators and predictors of response to radiotherapy and chemotherapy in selected tumor types.

The role of miRNAs in major tumor cell processes is addressed by three contributions. Dr. Profumo and Dr. Gandellini extensively review the role exerted by specific miRNAs in the different steps of tumor dissemination and metastasis formation and highlight
the most relevant issues to be solved in view of the clinical exploitation of miRNA-based approaches for prevention and treatment of the metastatic disease. Dr. Schepeler reviews currently available information on the cross talk between miRNAs and the Wnt signaling network, which is of crucial importance for the development of mammalian cells and in pathological conditions including cancer. Finally, Dr. Bilsland and colleagues discuss the role of miRNAs in the regulation and induction of senescence, a cellular process that recently attracted renewed interest in view of its potential as a therapeutic target for cancer therapy.

In summary, the reviews in this issue highlight the relevance of miRNAs for cancer and provide a critical evaluation of their possible role in the management of cancer patients—as novel biomarkers and therapeutic targets/tools—in years to come.

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