

Preface

The Nobel Prize in Physiology or Medicine could have been awarded to Victor Ambros, David Baulcombe and Gary Ruvkun in 2013; however, it did not come to fruition but it is my belief that these investigators may receive such honor in future years to come. Since the discovery of microRNA (miRNA) some 20 years ago, these three scientists worked to uncover the mystery of miRNA, the small segments of nucleotides that silence genes. While studying the development of the nematode worm, Ambros and Ruvkun discovered miRNA in animals, while Baulcombe discovered it in plants. Since their discovery, it took more than two decades to fully appreciate the value of miRNA in human health and diseases. The literature search conducted recently showed about 11,000 articles on “miRNA and Cancer” while “cancer specific miRNA” search yielded only about 2,500 articles; however, “miRNA targeted therapy” showed about 500 articles although not all appears to be directly relevant to miRNA targeted therapy. The rapid growth seen especially in the last decade in the field of miRNA research clearly suggests that this is a very attractive field in biomedical research although we need to harness the fruit of this cutting-edge research area for cancer targeted therapy, which became the subject of the new book as illustrated below.

Activation of oncogenes and/or the inactivation of tumor suppressor genes are known to contribute to the development of tumors as well as progression of disease to a metastatic state. The regulation of genes is by far controlled by many transcription factors which are often deregulated during the development and progression of cancer. In addition, emerging evidence clearly suggests that the deregulation of microRNAs (miRNAs) or small non-coding RNAs could also regulate the expression of genes. Likewise, miRNA genes are also regulated by transcription factors. It is well known that miRNAs are a major class of small, noncoding RNA molecules that regulate gene expression by targeting mRNAs to trigger either translational repression or mRNA degradation. The most attractive feature of miRNA is that one miRNA can regulate many target mRNAs, and thus miRNA targeted therapy is highly promising because multiple genes could be regulated by targeting a single miRNA, which becomes very important for the killing of highly heterogeneous populations of cancer cells within a tumor mass. Moreover, miRNAs

have recently been more widely investigated due to their potential role as targets for cancer therapy especially for targeted elimination of cancer stem cells (CSCs) because the CSCs are the cells that are believed to be highly resistant to conventional therapeutics, and thus responsible for tumor recurrence and metastasis. Therefore targeted elimination of CSCs through targeting miRNAs appears to be highly promising to eradicate human malignancies. The chapters presented in this book are focused on discussing the role of miRNAs in the regulation of cancer cell function during tumor development and progression, which will arm us with knowledge that will allow us to design miRNA targeted cancer therapy in the near future, especially for overcoming therapeutic resistance which will drastically improve the treatment outcome of patients diagnosed with cancer.

In this book, we are providing an overview and an update of our current understanding of the mode of action of several of these well characterized miRNAs in human cancers and document known strategies for the development of miRNA targeted therapeutics. It is anticipated that this special book would stimulate further research in the field and educate young scientists to generate stimulating ideas for novel discovery towards de-programming or re-programming of genes through targeting miRNAs that are either silenced or activated in cancer, and such mechanistic insight would serve as a novel approach for the prevention and/or treatment of most human malignancies.

The first and the second chapter rightly focused on glioma and glioma stem cells as described by the laboratory of Drs. Mittal and Brodie, respectively. The next three chapters are focused on lung cancer and dedicated to tumor recurrence, drug resistance, and lung cancer stem cells by Drs. Gong, Ochiya and Ahmad, respectively. Next, Dr. Abdelmohsen's group has summarized the knowledge of miRNA in ovarian cancer diagnosis and therapy followed by a presentation by Dr. Banno and colleague who described the application of miRNA in the treatment and diagnosis of cervical cancer. The next chapter is focused on colorectal cancer and drug resistance as well as the biology of tumor recurrence as discussed in the chapter presented by Dr. Majumdar and his colleague. This is followed by chapters on liver cancer, renal cancer and pancreas cancer presented by Drs. Galle, Majid, and Cordelier, respectively. The next chapter is from the laboratory of Dr. Sarkar focusing on the role of miRNA in drug resistance, EMT, and cancer stem cells, both in prostate and pancreas cancer. The next two chapters are focused on thyroid cancer and pediatric solid tumors as presented by Drs. Kimura and Segura, respectively. The next three chapters are not focused on any particular tumor system, rather these are focused on general topic covering the aspects of immunology, DNA repair system, and the molecular signaling associated with VEGF and its receptor in the context of miRNA as presented by Drs. Hong and Farooqi, respectively. The last chapter, contributed by Dr. Azmi and his colleagues, is the latest in the field of system biology and network modeling and how these tools could be useful in understanding the complexities of miRNA networks. As such, this field would become the future of miRNA research toward the development of targeted therapy. Although not explicitly stated, the field of cell-cell communication, exosome and miRNA is an active area of research and some of chapters, especially Chapter 2

invoked their roles in the biology of cancer development and progression; however, focused chapters on this topic would be an important future project. A variety of cells release membrane vesicles, such as exosomes that are thought to play key roles in cell–cell communication by transportation of miRNAs. There have been some efforts to use exosomes as a carrier of miRNAs toward miRNA targeted therapy because exosomes provide for stability of miRNA in the body fluid and carry the functional miRNAs in remote cells. Furthermore, recent studies have demonstrated that the modification of ligands on the exosomal membrane permits the accumulation of the exosomes to target tissues such as cancer and the delivery of the therapeutic miRNAs into the target cells. This concept would provide, in the future, an overview of the potential roles of exosomes with respect to carrier of therapeutic miRNAs for miRNA targeted therapy, which awaits further exploration.

Finally, I would like to thank the Springer publishing group for their trust in me for organizing this special topic on the emerging role of miRNA in cancer therapy in the book entitled *MicroRNA Targeted Cancer Therapy*. This book illustrates the complexities of the regulation and deregulation of genes mediated through miRNAs and how miRNAs could be targeted for cancer therapy as documented by a series of chapters compiled in this book as stated above. It is hoped that targeting miRNAs will not only target cancer cells and CSCs but it will also target the tumor microenvironment (more like the entire tumor environment such as the entire host; especially the exosome mediated re-distribution of miRNAs occurs in human) for enjoying the benefit of better treatment outcomes for patients diagnosed with cancer toward achieving the objectives of complete eradication of cancer. This book provides the tip of the iceberg of the collection of chapters on the state of our knowledge on miRNA in cancer and targeted therapy. This knowledge would likely be useful for bringing newer generations of scientists with broader perspectives in launching cutting-edge innovative molecular research and drug development that will certainly help in designing targeted clinical trials in order to realize the dream of targeted therapy for eradicating human malignancies.

In closing, I would like to thank all the authors for their cooperation, hard work, and talented contributions to bring this book to the readers in a timely fashion. I sincerely hope that the content of this book will be useful in educating younger scientists in the field of “miRNA and cancer” research so that they can carry the torch in innovative research to rip the benefit of miRNA targeted cancer therapy for better treatment of human malignancies. Finally, I would like to dedicate this book to my lovely wife, Arfatun H. Sarkar and my three wonderful children, Sarah, Sanila and Shaan for their understanding, unconditional love, support, and sacrifice to enhance my scientific career.

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