Preface

Only 20 years after the discovery of small non-coding, single-stranded ribonucleic acids, so-called microRNAs (miRNAs), as post-transcriptional gene regulators, the first miRNA-targeting drug Miravirsen for the treatment of hepatitis C has been successful in clinical phase II trials. Addressing miRNAs as drug targets may enable the cure of diseases, which presently seems impossible. However, due to miRNAs' chemical structure, generation of potential drug molecules with necessary pharmacokinetic properties is still challenging. Thus, Miravirsen remains an exception. In conclusion, drug target miRNA requires innovation at the level of drug discovery.

Until today, several approaches have been developed to modulate miRNAs' function in the hope of potential therapeutic use. After a short introduction to the field of miRNA drug discovery (Chapter 1) and to miRNA target identification (Chapter 2), the book summarizes the three strategies to overcome pharmacodynamics and pharmacokinetics challenges: Firstly, due to their poor cell permeability, anti-sense agents targeting miRNA are applied in advanced formulations, or are chemically optimized to increase their delivery (Chapters 3–9). Secondly, efforts were made to develop small molecule miRNA modulators to overcome anti-sense agents' limitations (Chapters 10–11). Especially, DICER-mediated miRNA maturation is a target for small molecules. General enhancers of miRNA maturation, as well specific substrate inhibitors, were identified, thereby demonstrating the potential of adopting the concept of small molecules to target miRNA functions (Chapters 12–14). Thirdly, as miRNA function is executed by the Argonaute 2 protein, new chemical entities, addressing this protein (or its complex with target miRNA of interest) with likely better pharmacokinetic parameters than reported oligonucleotides, may open new perspectives in miRNA drug discovery (Chapters 15–21).

Regarding the enormous potential of miRNAs in drug discovery, my motivation to edit this Methods in Molecular Biology volume was not to give an overview of existing challenges but rather to provide a concise technical manual of recently developed approaches to overcome these challenges in miRNA drug discovery to open new ways in therapies. Therefore, I am thankful to all contributors, leading practitioners from academia and industry, of the chapters in this book for their outstanding effort and commitment to this project. I would also like to thank Prof. John Walker for his encouragement. Additional thanks go to the staff at Springer Science + Business Media for their excellent support.

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