

Preface

MY FIRST EXPOSURE TO RNA INTERFERENCE (RNAi) came at a Pew Scholars meeting in Puerto Vallarta, Mexico in 1998. Craig Mello gave a short, informal talk about a remarkable observation—exposing *Caenorhabditis elegans* to double-stranded RNA (dsRNA) caused potent and sequence-specific silencing of homologous genes. Beyond this, the response to dsRNA had a number of nearly unbelievable properties. Silencing occurred not only in cells directly exposed to the dsRNA, but also spread throughout the organism and into its progeny. We were all confounded and amazed by this seemingly inexplicable set of observations.

I am fairly certain that, at the time, Craig had not yet realized the extent to which his observations would take hold of biology to create an exciting new field, which at the time of the writing of this book, seems to be expanding at an exponential rate. Shortly after the original report of RNAi, Rich Carthew, another Pew Scholar, extended many of Andrew Fire's and Mello's basic observations about the ability of dsRNA to suppress gene expression into *Drosophila* embryos. Biochemical and genetic studies led to the realization of a common silencing response that extended throughout eukaryotes from plants (where the phenomena were really first noted) to fungi to animals.

Since its inception, the study of RNAi has proceeded along two parallel tracks. The first is an effort to understand the biology of this response—its mechanism and its role in the organism. The second has been the desire to develop RNAi as an experimental and possibly therapeutic tool. This duality has made the planning and construction of this book a challenge. In the end, it was decided that the volume should provide both an introduction to the biology of RNAi and practical advice, including detailed protocols, on its application in numerous systems.

The work described herein represents a field that is moving at an astonishing pace. Therefore, I am all the more grateful to the authors, who took time from their very busy schedules to contribute to this volume. This book would also not have been possible without the constant support (read nagging and prodding) of the people at Cold Spring Harbor Laboratory Press, namely, Mary Cozza, Judy Cuddihy, David Crotty, and John Inglis. I am also indebted to those colleagues in the field who have provided encouragement and support of our work over the past several years. I am especially thankful for the talented group of graduate students and postdoctoral fellows including Scott Hammon, Emily Bernstein, Yvette Seger, Amy Caudy, Ahmert Denli, Jian Du, Izabela Sujka, Jose Silva, Patrick Paddison, Doug Conklin, and Michelle Carmell. I am grateful to my family, Gretchen, Will, and Claire, for their support and tolerance of the time that this endeavor has consumed.

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