Protein Synthesis and Translational Control

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EDITED BY

John W.B. Hershey
University of California, Davis

Nahum Sonenberg
McGill University

Michael B. Mathews
UMDNJ–New Jersey Medical School

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Front cover artwork: The cover art depicts the structure of the eukaryotic ribosome from the yeast *Saccharomyces cerevisiae*. The ribosome consists of four RNA chains (gray ribbons) and 79 different proteins (colored ribbons). With a total mass of 3.3 MDa, it is more intricate and ~40% larger than its bacterial counterpart. The previous edition of the translational control series, *Translational Control in Biology and Medicine* (2007), showed the structure of the bacterial ribosome on its cover. The display of the structure of the eukaryotic ribosome on the cover of this volume is a demonstration of the recent remarkable advances made in the protein synthesis field. The image was kindly provided by Marat Yusupov, Directeur de Recherche du CNRS.

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Preface

THE MECHANISM OF PROTEIN SYNTHESIS and its regulation have been studied intensively for more than a half-century, yet much remains to be learned. This is a particularly exciting time for such studies, as the role of translational control in regulating gene expression is broadly recognized as more important than previously thought. In the past, many studies focused on defining the translational machinery and how it functions. The translation of specific mRNAs suspected of being regulated was also studied, establishing a variety of mechanisms for controlling the translational efficiency of mRNAs. During the past few years, high-throughput methods have been applied to studies of translational control, resulting in the realization that such regulation is applied to the majority of mRNAs. Situated at the nexus between nucleic acids and proteins, the importance of translational control, now appreciated for its role in establishing the cell's proteome, is comparable to that of transcriptional control—a realization that makes studies of translational control even more compelling and essential.

The fact that protein synthesis is regulated broadly means that we need to understand a vast range of translational controls that operate on most mRNAs. This is an enormous challenge, as mRNAs differ in structure, in their modes of initiation, and in the assortment of *cis*-acting sequences that coordinate different regulating elements. Many mRNAs are themselves a collection of different structures due to alternative promoters, splicing, or processing. In addition, multiple regulatory mechanisms may operate on individual mRNAs, complicating their identification. To address this problem effectively, a precise knowledge of the mechanism of protein synthesis is required. Recent advances in ribosome structure, single-molecule studies, and reaction kinetics should provide the depth of understanding required to explain regulation.

While we were contemplating editing a fourth edition of *Translational Control*, John Inglis suggested that we consider creating a book for the Perspectives series for the Cold Spring Harbor Laboratory Press. Our previous editions, namely *Translational Control* (1996), *Translational Control of Gene Expression* (2000), and *Translational Control in Biology and Medicine* (2007), provided comprehensive reviews of the process and regulation of protein synthesis. For the Perspectives series, we have attempted to focus on the current status of the field, with emphasis on aspects that need further elucidation and development. We have chosen a limited number of specialized areas that we feel are particularly important for future developments in the field. The volume begins with a number of chapters that examine fundamental mechanisms of protein synthesis and continues with chapters that describe approaches or mechanisms that apply broadly to many mRNAs. A number of chapters address a specific aspect of cell metabolism where translational control plays a prominent role. The volume ends with an examination of how insights into translational control can be used to develop therapeutic agents.

We thank all of the authors for their superb efforts in generating thoughtful and exciting chapters. The quality of the book rests on their efforts. We also thank John Inglis and Richard Sever for their encouragement, project manager Barbara Acosta for her competent and tireless attention to our submissions, and the production staff of the Press.

JOHN W.B. HERSHEY
NAHUM SONENBERG
MICHAEL B. MATHEWS