Preface

As the mysteries stored in our DNA have been more completely revealed, scientists have begun to face the extraordinary challenge of unraveling the intricate network of protein–protein interactions established by that DNA framework. It is increasingly clear that proteins continuously interact with one another in a highly regulated fashion to determine cell fate, such as proliferation, differentiation, or death. These protein–protein interactions enable and exert stringent control over DNA replication, RNA transcription, protein translation, macromolecular assembly and degradation, and signal transduction; essentially all cellular functions involve protein–protein interactions. Thus, protein–protein interactions are fundamental for normal physiology in all organisms. Alteration of critical protein–protein interactions is thought to be involved in the development of many diseases, such as neurodegenerative disorders, cancers, and infectious diseases. Therefore, examination of when and how protein–protein interactions occur and how they are controlled is essential for understanding diverse biological processes as well as for elucidating the molecular basis of diseases and identifying potential targets for therapeutic interventions.

Over the years, many innovative biochemical, biophysical, genetic, and computational approaches have been developed to detect and analyze protein–protein interactions. This multitude of techniques is mandated by the diversity of physical and chemical properties of proteins and the sensitivity of protein–protein interactions to cellular conditions. In order to provide scientists with practical tools to address their vital biological questions in the post-genome era, *Protein–Protein Interactions: Methods and Applications* presents a collection of frequently employed techniques for identifying protein interaction partners, qualitatively or quantitatively measuring protein–protein interactions in vitro or in vivo, monitoring protein–protein interactions as they occur in living cells, and determining interaction interfaces. It is hoped that this book will be useful to a broad spectrum of researchers who are interested in studying protein–protein interactions in various systems.

Protein–Protein Interactions: Methods and Applications consists of five sections. It begins with two concise overviews of the fundamental principles of protein–protein interactions. They illustrate the structural diversity of protein interactions and some common experimental design considerations that are important for quantification of these interactions. Part Two describes a wide range of biochemical and biophysical methods for detecting and measuring protein–protein interactions in vitro. Commonly used spectroscopic, electrophoretic, and affinity matrix–based techniques are presented, many of which allow quantitative analysis of protein–protein interactions. This section ends with tools for analyzing structural interfaces and the design of peptide inhibitors of protein interactions. Advances in genetics and molecular biology have revolutionized the way that we study protein–protein interactions. Part Three reflects these changes and covers popular methods for studying protein–protein interactions in heterologous cell systems, including various bacterial, yeast, and mammalian two-hybrid systems and co-immunoprecipitation studies. These methods provide a simple solution for analyzing protein–protein interactions in an in vivo environment. Part Four presents state of the art methodologies to monitor protein–protein interactions in living cells, including applications using the fluorescence resonance energy transfer (FRET) technology. These approaches share a common bond in that they allow the capture and visualization of protein–protein interactions as they occur. In the post-genome age, it is expected that conventional methods for studying protein–protein interactions will still play an important role. However, it is hoped that proteomics and bioinformatics-based approaches will be rapidly developed to study protein–protein interactions on a large scale. Part Five begins to address this issue, focusing on high-throughput methods and on computational approaches. This section ends with a tutorial on using Internet resources, which serves as a springboard to additional information and techniques for studying protein–protein interactions.

Both basic and clinical researchers will find this book valuable for its broad coverage from simple affinity-based pull-down assays to cutting edge technologies such as FRET and solid-phase isotope tagging–based mass spectrometry. The basic theory and practical application of these widely used, representative methods are described in detail by experienced researchers. Examples are also incorporated to illustrate each method, along with notes and explanations for sensitive procedures and potential pitfalls. These features, together with our broad coverage of the topic, are designed to empower readers in their quest to decipher the functions of proteins and complex biological regulatory systems.

It is truly a great pleasure to put together a book on this important, exciting, and timely topic! I have been privileged to work with the many leaders in the protein–protein interaction field who willingly contributed their valuable time and effort to making this book possible. I am grateful to each of the contributors for their enthusiasm and tremendous efforts and to John Walker, the series editor, and Craig Adams, James Geronimo, and all at Humana Press for their guidance. My sincere thanks go to Shane Masters, Keith Wilkinson, and Jonathan Cooper for their invaluable advice and suggestions and to Lisa Cockrell and Robert Fu for assistance in preparing this book. Finally, I express my deepest appreciation to Robert, Emily, and Guo-hua, who provide constant encouragement and support.

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