

Chapter XXXIX

Protein Interactions and Diseases

Athina Theodosiou*

Biomedical Research Foundation of the Academy of Athens, Greece

Charalampos Moschopoulos*

Biomedical Research Foundation of the Academy of Athens, Greece

Marc Baumann

Biomedicum, Helsinki University, Finland

Sophia Kossida

*Biomedical Research Foundation of the Academy of Athens, Greece,
and Biomedicum, Helsinki University, Finland*

ABSTRACT

In previous years, scientists have begun understanding the significance of proteins and protein interactions. The direct connection of those with human diseases is now unquestionable and proteomics have become a scientific section of great research interest. In this chapter, we present a detailed description of the nature of protein interactions and describe the more important methodologies that are being used for their detection. Moreover, we review the mechanisms leading to diseases and involving protein interactions and refer to specific diseases such as Huntington's disease and cancer. Lastly, we give an overview of the most popular computational methods that are used for the prediction or the healing of the diseases.

INTRODUCTION

The recent completion of many genome-sequencing projects of various organisms, from viruses to mammals, is undoubtedly the greatest triumph of molecular biology since the discovery of the DNA double helix. After the complete genome sequencing of many organisms, including human, the focus

of molecular biology has gradually shifted the interest from genomes to proteomes, in order to explore and discover the function of proteins (Eisenberg *et al.*, 2000; Pandey *et al.*, 2000).

One of the great challenges in the protein field is to reconstruct the complete protein interaction network within the cells, the so-called interactome. There is great difficulty in achieving this goal as the nature of the protein interactions varies depending on many environmental conditions that affect the cell (Nooren *et al.*, 2003). However, due to the fact that protein interactions play a vital role in the basic functions of an organism's cell, analysis of these networks will unravel the secrets of the pathways in which the under question interactions are detected and ultimately provide insights in how diseases are developed (Sam *et al.*, 2007).

Several methods, which will be detailed within this book chapter, exist for the detection of protein interactions. During the last years, new high-throughput methodologies are being used to detect a great amount of protein interactions with a single experiment (Piehler 2005). Unfortunately, these methods are error-prone, therefore the generated data need further analysis (Droit *et al.*, 2005). Today, large amounts of protein interactions of many organisms are stored in large on-line databases and are available for academic purposes.

These data are useful in order to better understand the connection between protein interactions and diseases (Chen 2006). In this chapter, we present a detailed description of protein interactions and a full overview of the approaches taking advantage of these, to better understand specific diseases.

The chapter is organized as follows: the first section reviews the nature of protein interactions and various experimental and computational methods for detecting and predicting those. The most important databases used for storing and integrating protein interactions and protein interactions associated with disease are described, whereas the recent information about the human interactome is mentioned. The second section describes mechanisms of protein interactions that have been shown to lead to disease and the third section describes the computational methods that are used for the holistic understanding of specific diseases.

PROTEIN INTERACTIONS

Introduction

One of the goals of system biology is to understand the behaviour of the biological systems by studying the molecules that are involved in them. Therefore, it is of great importance to determine the interactions taking place among the molecules. The study of protein interactions has been vital to the understanding of how proteins function within the cell, in where proteins interact with other proteins, metabolites and nucleic acids. More specifically, protein interactions are crucial for forming structural complexes, for extra-cellular signalling, for intra-cellular signalling, for cell communication and for several other aspects of cellular function.

The characterization of protein interactions is really important to understand the molecular mechanism of biological pathways and disease processes. Complete knowledge of these pathways will help us to understand how diseases, such as cancer, develop. Since almost all processes are regulated by multiple complexes, the absence of some interactions or the complete absence of physical interactions can be the cause of disease in humans (Ryan and Matthews, 2005).

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