

Preface

When I was invited to edit this volume on posttranslational modifications (PTM) of proteins in health and disease, and after nearly 30 years of uninterrupted teaching of molecular biology of the cell and signal transduction phenomena, I knew the challenge that awaited me, considering the enormous variety of PTM that proteins can undergo, their tremendous importance for normal cell biology, and their requirement for keeping tissues in a healthy state. Nevertheless, I decided to accept the invitation as a means of learning from experts what I try to teach to my students.

Although the first step in protein diversification occurs at the transcriptional level, by mRNA splicing, the PTM of proteins at one or more sites is the way by which the number of protein variants in cells is greatly increased, so that their quantity exceeds by two to three times the number of proteins predicted by the DNA coding capacities of cells. More than 500 human protein kinases, 150 protein phosphatases and 500 proteases are engaged in protein modifications; about 5% of our genetic material encodes enzymes that intervene in PTM of proteins, and at least 1% encodes enzymes involved in the glycosylation process.

Posttranslational modifications serve many different purposes in a wide variety of cellular processes, such as protein synthesis, folding, stability, the housing of prosthetic groups, vesicular trafficking, protein targeting to particular cell stores, exocytosis and endocytosis, the biogenesis of cell organelles and basal lamina, as well as signal transduction with functional effects for enzyme regulation and metabolic control on the one hand, and for gene expression, cell division, differentiation and apoptosis on the other.

The enormous variety and versatility of the protein modifications, which may drive permanent or transient changes in conformation and physicochemical properties of the respective protein, represent a great challenge for proteomic research. There are two broad classes of covalent modifications in proteins. The first corresponds to enzyme-assisted covalent addition (or elimination) of a chemical group, frequently an electrophilic fragment of a cosubstrate, to a side chain residue in a protein. The modified side chain is usually electron-rich and acts as the nucleophile in the transfer. The second class of PTM is the covalent cleavage of peptide fragments in proteins driven by proteases or, less frequently, by autocatalytic cleavage. Phosphorylation and dephosphorylation of proteins with their gain and loss of function, glycosylation and its role in appropriate protein sorting, and secretion-associated

proteolysis are the most studied topics, but further modifications, such as protein lipidation, prenylation, glypiation, acetylation, methylation, oxidation, hydroxylation, nitrosylation, sulfurylation, ubiquitinylation, sumoylation, ADP-ribosylation, the degradation of basal lamina components, prosthetic group tethering and other protein changes, are also required for essential cellular functions.

Since our current knowledge of protein PTM, including their nature and biological significance, probably only covers a small fraction of the modifications responsible for building the whole cell proteome, the goal of the present volume was to provide the reader with several updated reviews that stimulate further investigations in the proteomic field. The present volume compiles nineteen reviews focused on functional and pathological aspects of protein prenylation, the incorporation of glycosylphosphatidylinositol (GPI) moieties, oxidation, nitrosylation, glycosylation, and phosphorylation and dephosphorylation, with emphasis on their outcome for protein–protein interaction phenomena and down-stream effects. Three additional chapters are devoted to protein ubiquitination, sumoylation and endoplasmic reticulum-associated degradation (ERAD), and three more to the influence on histone modification for gene expression and DNA repair. The last two chapters are focused on proteolytic processing of intracellular and basal lamina proteins. The list of topics covered is far from complete; their selection should not be understood in the sense of merit or importance but as the result of practical limitations in the scope and assembly of this work.

The chapters of this book have been written by eminent experts to whom I have to express my most sincere gratitude. I also want to thank Dr. M. Zouhair Atassi, the publisher, Ms. Stephanie Jakob, the editor, and the Fundación Séneca de la Región de Murcia for making this work possible. I must also thank my colleagues and associates Drs. Encarnación Muñoz-Delgado, Francisco J. Campoy and María Fernanda Montenegro-Arce for their help and encouragement. I must also thank my son and daughters Federico, Ana Victoria and Belén for their patience, my little grandson Federico for his tenderness, and finally my wife María Jesús for her ability to make my life easier and happier every day.

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