

Contents

Contributors	xi
Preface	xv

1. Posttranslational Modifications of Proteins and Their Role in Biological Processes and Associated Diseases

IRFAN-UR-RAUF TAK, FASIL ALI, JEHANGIR SHAFI DAR, AQIB REHMAN MAGRAY,
BASHIR A. GANAI, M.Z. CHISHTI

1 Introduction	1
2 Major Posttranslational Modifications	4
3 Functions of Posttranslational Modifications	15
4 Diseases Associated With Posttranslational Modifications	19
5 Role of Posttranslational Modifications in Protein-Protein Interaction	21
6 Role of PTMs in Replication	22
7 Role of PTMs in Transcription	25
8 Role of PTMs in Translation	27
9 Chemical and Functional Aspects of Protein PTMs	28
10 Role of PTMs in Histone Modification	29
11 Conclusion and Future Prospectus	31
References	32
Further Reading	35

2. Clinical Perspective of Posttranslational Modifications

IRAM ASHAQ KAWA, AKBAR MASOOD, SHAJRUL AMIN, MIR FAISAL MUSTAFA,
FOUZIA RASHID

1 Introduction	37
2 Glycosylation	38
3 Acetylation	43
4 Phosphorylation	45
5 Carbonylation	46
6 Methylation	47
7 Hydroxylation	49
8 Nitration	51
9 Sulfation	52
10 Palmitoylation	53
11 Conclusion and Future Perspective	58
References	58

3. Phosphorylation and Acetylation of Proteins as Posttranslational Modification: Implications in Human Health and Associated Diseases

SANA QAUSAIN, HEMALATHA SRINIVASAN, SHAZIA JAMAL, MOHAMMAD NASIRUDDIN, MD. KHURSHID ALAM KHAN

1 Introduction	69
2 Phosphorylation	70
3 Protein Acetylation	77
4 Conclusion and Future Prospects	81
References	81

4. Protein Modifications and Lifestyle Disorders

SHIVANI ARORA, ANJU KATYAL

1 Introduction	87
2 Deregulated Adipocyte Proteome in Obesity	88
3 Proteostasis in Diabetes	92
4 Protein Modification in Cardiovascular Diseases	94
5 Modified Proteome in Rheumatoid Arthritis	97
6 Conclusion and Future Aspects	101
References	102
Further Reading	108

5. Ubiquitin Mediated Posttranslational Modification of Proteins Involved in Various Signaling Diseases

LAVANYA V, SHAZIA JAMAL, NEESAR AHMED

1 Introduction	109
2 Ubiquitination in Inflammatory Pathways	111
3 Implications of UPS in Cancer	112
4 E3 Ligases in Diabetic Retinopathy (DR)	118
5 Implications of UPS in Neurodegenerative Diseases	119
6 Implications of UPS in Renal Disorders	122
7 Conclusion and Future Perspectives	123
References	125

6. Role of Glycosylation in Modulating Therapeutic Efficiency of Protein Pharmaceuticals

PARVAIZ AHMAD DAR, USMA MANZOOR, SNOWBER SHABIR WANI, FASIL ALI, TANVEER ALI DAR

1 Introduction	131
2 Challenges Associated With Protein Pharmaceuticals	132
3 Protein Glycosylation and Its Pharmacological Significance	134

4 Modulation of Therapeutically Important Properties of Proteins by Glycoengineering	135
5 Conclusion and Future Direction	139
References	140

7. Posttranslational Modification of Heterologous Human Therapeutics in Plant Host Expression Systems

APPAGARI ARCHANA, LAKSHNA MAHAJAN, SAFIKUR RAHMAN, RINKI MINAKSHI

1 Introduction	145
2 N-Glycosylation as a Major Posttranslational Modification	147
3 Factors Affecting the Natural Glycosylation of Plant-Farmed Human Pharmaceuticals	149
4 Plant Cell Culture Versus Whole Plant Cultivation for Biopharmaceutical Production	152
5 Developing Humanized and Improved Glycoproteins	154
6 Glycoengineering: Concept of "Biobetters" and "Biosimilars"	156
7 Success Stories	157
8 Ebola Virus Infection	158
9 Gaucher's Disease	158
10 Monoclonal Antibodies	158
11 Vaccines	159
12 Benefits of Plant Expression System	159
13 Limitations of Plant Expression System	160
14 Conclusion and Future Prospects	161
References	162

8. Protein Modification in Plants in Response to Abiotic Stress

HILAL AHMAD QAZI, NELOFER JAN, SALIKA RAMAZAN, RIFFAT JOHN

1 Introduction	171
2 Abiotic Stress in Plants	172
3 Types of Abiotic Stress in Plants and the Proteins Involved Therein	174
4 Protein Modification in Plants in Response to Stress	184
5 Conclusion and Future Perspective	189
References	190
Further Reading	199

9. Posttranslational Modifications Associated With Cancer and Their Therapeutic Implications

ANIKET KUMAR BANSAL, LAISHRAM RAJENDRAKUMAR SINGH, MAJID RASOOL KAMLI

1 Introduction	203
2 Posttranslational Modifications That Regulate the Mdm2-p53 Interaction	204
3 Modification of Retinoblastoma Tumor Suppressor Protein (pRB) and Its Association to Cell Cycle Progression	206

4 Regulation of NF- κ B by Various Posttranslational Modifications	207
5 Regulation of Gene Expression Via Histone and Histone Deacetylase Modifications	209
6 Deregulation of Tyrosine Kinase by Posttranslational Modifications	211
7 Posttranslational Modifications in Ras/Raf/MEK/ERK in MAPK Pathway	212
8 Modification of Signal Transducers and Activators of Transcription	214
9 Phosphorylation of Cyclin-Dependent Kinases and Their Therapeutic Implications	215
10 Posttranslational Modification in Cadherins	218
11 Prenylation and G-Protein Coupled Receptors	219
12 Summary and Future Perspectives	220
References	221

10. Nonenzymatic Posttranslational Protein Modifications: Mechanism and Associated Disease Pathologies

SHEEZA KHAN, AJAZ A. BHAT

1 Introduction	229
2 Carbamylation	230
3 Carbonylation	237
4 N-Homocysteinylation	244
5 S-Nitrosylation	246
6 Glycation	253
7 Summary	262
Acknowledgment	262
References	263

11. Protein Covalent Modification by Homocysteine: Consequences and Clinical Implications

GURUMAYUM SURAJ SHARMA, RESHMEE BHATTACHARYA, LAISHRAM RAJENDRAKUMAR SINGH

1 Introduction	281
2 Homocysteine and Protein Homocysteinylation	282
3 Protein S-Homocysteinylation	283
4 Protein N-Homocysteinylation	285
5 Homocystinuria/Hyperhomocysteinemia: Condition Persisting for Protein Modifications	292
6 Clinical Complications Associated With Elevated Hcy	294
7 Conclusions and Future Prospects	304
References	304
Further Reading	311

12. Posttranslational Modifications in Algae: Role in Stress Response and Biopharmaceutical Production

PARVEZ AHMAD, FAREHA BANO

1 Introduction	313
2 Posttranslational Modifications in Algae With Respect to Stress Response	314
3 Posttranslational Modification of Therapeutic Proteins in Microalgae	323
4 Conclusion and Future Prospects	330
References	331
Further Reading	337

13. Protein Glycosylation: An Important Tool for Diagnosis or Early Detection of Diseases

HUMAYRA BASHIR, BARQUL AFAQ WANI, BASHIR A. GANAI, SHABIR AHMAD MIR

1 Introduction	339
2 Protein Posttranslational Modifications and Quest for Clinical Biomarkers	340
3 Protein Glycosylation and Related Disorders	341
4 Technological Approaches in Analysis of Protein Glycosylation	346
5 Conclusions and Future Prospectus	350
References	351
Further Reading	358

Index	361
-------	-----