

Contents

1	DNA Replication	1
1.1	The Mechanism of DNA Replication	1
1.2	Classification and Structure of DNA Polymerases	3
	Further Reading	3
2	Disturbances of the DNA Replication System	5
2.1	DNA Damage Blocks DNA Replication	5
2.2	DNA Damage Increases Misincorporation Ratio	7
2.3	DNA Damage Forms Frameshift During DNA Replication	8
2.4	DNA–DNA Cross-Linking Destroys DNA Replication	10
	Further Reading	11
3	Fate of DNA Replisome upon Encountering DNA Damage	15
3.1	The DNA Replisome of <i>E. coli</i> , T7 and T4	15
3.2	The <i>E. coli</i> DNA Replisome Bypassing DNA Damage	16
3.3	The T4 DNA Replisome Bypassing DNA Damage	17
3.4	The T7 DNA Replisome Bypassing DNA Damage	18
	Further Reading	18
4	External Causes for DNA Damage	21
4.1	Environmental Carcinogens	21
4.2	Formation of DNA Damage After Exposure to Environmental Carcinogens	21
4.3	Disease, Cancer, and Tumor Resulted from Environmental Carcinogens	24
	Further Reading	24
5	Effect of Environmental Carcinogens on Cellular Physiology	27
5.1	Overview of Biological Activities of Cells	27
5.2	Cell Cycle	28

5.3	Cell Proliferation and Apoptosis	29
5.3.1	Cell Apoptosis	29
5.3.2	Cell Proliferation	29
5.3.3	Gene Expression.	31
5.3.4	Cell and Tissue	32
	Further Reading.	32
6	Protocols for Studies of Bypass of DNA Damage	
	by DNA Polymerase	35
6.1	Introduction	35
6.2	Kinetic Analysis of Bypass of DNA Damage	36
6.2.1	Materials.	36
6.2.2	Preparation of Reaction Buffer.	36
6.2.3	Preparation of Reaction Quench Buffer.	36
6.2.4	Preparation of Primer/Template that Contains DNA Damage at Incorporation Position	36
6.2.5	Analysis of DNA Incorporation Product	36
6.2.6	Primer Extension Assay with All Four dNTPs.	37
6.2.7	Steady-State Kinetic Analyses	37
6.2.8	Pre-steady-state Reactions	37
6.2.9	Pre-steady-state Trap Experiments.	38
6.2.10	Phosphorothioate Analysis.	38
6.2.11	Stopped-Flow Fluorescence Measurements of Conformational Change.	38
6.2.12	Kinetic Simulations	39
6.3	LC-MS/MS Sequence Analysis of Extension Products Beyond DNA Damage	40
6.3.1	Materials.	40
6.3.2	Preparation Sample of DNA Extension Products Beyond DNA Damage	40
6.3.3	LC-MS/MS Sequence Analysis of Extension Products	40
6.4	X-Ray Crystal Structure Analysis of DNA Polymerase with DNA Containing DNA Damage.	41
6.4.1	Materials.	41
6.4.2	Crystallization of Polymerase with DNA Containing DNA Damage.	41
6.4.3	X-ray Diffraction Data Collection and Processing.	42
6.4.4	Structure Determination and Refinement.	42
	Further Reading.	42

DNA Replication - Damage from Environmental
Carcinogens

Zhang, H.

2015, XI, 43 p. 4 illus., 1 illus. in color., Softcover

ISBN: 978-94-017-7211-2