

# Index

- AAV. *See* Adeno-associated viruses
- Acyclovir  
drug resistance mutations, 501, 504–505  
mechanism of action, 498
- Adeno-associated viruses (AAV)  
DNA replication  
  initiator endonuclease, 800  
  origins, 804  
  replication proteins, 9–10  
  Rep protein role, 7, 9, 555–556, 802–803  
  rolling hairpin model, 3, 7, 9, 800–802  
  terminal resolution, 804  
genome, 7, 802–803  
life cycle, 799
- Adenovirus  
DNA polymerase  
  assay, 511  
  exonuclease, 704  
  helicase independence, 556  
  inhibitors, 511–512  
  precursor terminal protein complex, 511, 704–705  
  regulation, 515, 705–706  
  structure-function relationships, 512–513
- DNA replication. *See also* Terminal protein
- Ad-DBP single-stranded DNA-binding protein, 536, 700, 705–708  
  elongation, 11–13  
  initiation, 10–11, 91, 711  
  origin, 701  
  protein factors, 10, 142, 699–700  
  protein primer for DNA replication, 3, 141–142  
  sliding-back mechanism for transition from initiation to elongation, 145–146, 711–713  
  transcription factor stimulation  
    nuclear factor 1, 91–92, 142, 701–702, 708–710  
    octamer-binding transcription factor 1, 93–94, 142, 701–702, 710–711  
  genome, 10, 141, 699
- AL1  
ATPase activity, 839  
DNA binding, 839–841, 846  
gene, 837–838  
initiation of geminivirus replication, 837–842, 846  
nicking activity, 839, 847  
phosphorylation, 842  
transcriptional regulation, 841–842
- AL proteins. *See* AL1; Geminivirus
- Amplification, developmental  
  *Drosophila* chorion genes, 427–428, 955–956  
  *Sciara* DNA puffs, 428, 957–958
- AP endonuclease, base excision repair role, 252–253
- ARS. *See* Autonomously replicating sequence
- Autonomously replicating sequence (ARS). *See also* Origin complex  
  origins, 57, 65–66

- Autonomously replicating sequence  
(*continued*)  
simple origins, 50, 412, 440–441  
yeast  
  binding proteins, 887, 889–892  
  identification, 873  
  structure, 885–889  
5-Azacytidine, effect on replication  
  *timing*, 396
- Baculovirus  
  DNA replication  
    concatemer resolution, 868  
    mechanism, 861  
  origins  
    *hr* sequences, 857–860  
    independence of transfected DNA  
      replication, 866–867  
    mutants, 857  
    non-*hr* sequences, 860–861  
    role of multiple origins, 861–862  
    specificity between viruses, 867  
  required genes  
    DNA polymerase, 862–863  
    helicase, 863  
    *ie-1*, 864  
    *ie-2*, 865  
    *lef-7*, 866  
    *p35*, 865  
    *pcna*, 866  
    *pe-38*, 865  
    single-stranded DNA-binding  
      proteins, 864–865  
  gene expression, 856  
  genome, 855  
  types, 855
- Base excision repair, enzymes  
  AP endonuclease, 252–253  
  DNA deoxyribosephosphodiesterase, 253  
  DNA glycosylase, 250–252  
  DNA ligase, 253  
  DNA polymerases, 253  
  FEN-1, 253  
  poly(ADP-ribose) polymerase, 254
- B1 protein kinase. *See* Vaccinia virus
- Cdc6 kinase, replication control in yeast,  
  894–896
- Cdc7 kinase  
  DBF4 interaction, 894  
  S-phase promotion in yeast, 347–348,  
  893–894
- Cdks. *See* Cyclin-dependent kinases
- Cell cycle. *See individual phases*
- Cell growth  
  coordinating DNA replication and cell  
  growth, 331–332  
  independence from chromosome cycle,  
  332–333, 335  
  S-phase dependence, 333–334
- Chromatin  
  activated transcriptional states in yeast,  
  283–286  
  assembly  
    assay, 281  
    chaperones, 287  
    replication-dependent pathways,  
    279–281  
    replication-independent pathways,  
    279  
  DNA replication effect on structure  
    histone oligomers, 274–276  
    nucleosome, 273–276  
    regulatory complexes, 277–279  
  effect on replication speed, 19–20  
  helicase substrate, 565–566  
  nucleoprotein complex and  
    active/repressed states of  
    genes, 272–273  
  replication templates, 21  
  replication timing role, 286–287  
  repressed transcriptional states in yeast,  
  282–283  
  structure during cell cycle, 364  
  transcription factors, effect on struc-  
  ture, 88–89
- Chromosome. *See also* X chromosome  
  structure and replication  
    eukaryotes, 436–438  
    prokaryotes, 436–439  
  supercoil density, 451, 587
- Clb cyclins  
  activation by Cln cyclins,  
  342–343  
  M-phase promotion, 341–342  
  regulation during cell cycle, 341, 343–  
  344, 893  
  similarity with cyclin E, 358–359
- Cln cyclins  
  regulation during cell cycle, 341, 343–  
  344, 358  
  S-phase promotion, 341–344  
  synthesis, 356–357
- CMV. *See* Cytomegalovirus
- Crithidia fasciculata*. *See* Kinetoplast
- Cyclin D1  
  cell cycle regulation, 352–353, 358

- regulation by Rb, 358  
 synthesis, 356–357
- Cyclin-dependent kinases (Cdks)
- G<sub>1</sub>
- arrest with inhibitors, 333, 354–355
  - regulation, 346, 352–354
- G<sub>2</sub>-specific kinases, 360–361
- p40Sic1 inhibitor and S-phase onset, 346
- phosphorylation, 355
- primordial cell cycle regulation, 370–371
- rereplication prevention in yeast, 367–369
- S-phase promotion, 339–342, 360–361, 374–375
- Cyclin E
- cell cycle regulation, 353–354
  - similarity with Clb cyclins, 358–359
- Cytomegalovirus (CMV)
- DNA polymerase
- drug resistance mutations, 507–508
  - mapping of domain activities, 508
  - regulation, 514
  - structure, 506
- lytic replication origin, 728–729
- short replication transcripts, 728
- DBP. *See* Adenovirus
- DHFR. *See* Dihydrofolate reductase
- Dihydrofolate reductase (DHFR), Chinese hamster gene
- replication
- assays, 989, 995–996
  - origins of bidirectional replication
    - conformation, 994
    - footprinting, 995
    - genetic assays, 992–993
    - mapping, 988–992, 997
    - sequence, 994
  - timing, 989
  - transcription relationship to initiation, 996–997
  - staining, 989
- Dislocation mutagenesis, DNA polymerase fidelity, 229
- DnaA, initiation of replication, 442–443
- DNA deoxyribophosphodiesterase, base excision repair role, 253
- DNA glycosylase, base excision repair role, 250–252
- DNA helicase. *See* Helicase
- DNA ligase. *See also individual DNA ligases*
- active site, 575–576
  - assay
    - AMP dissociation by nicked DNA, 577–578
    - blunt-end joining, 579
    - formation of joined oligonucleotides, 578–579
    - ligation of nicked circular DNA, 579
    - pitfalls, 579–580
    - radiolabeling of enzyme/AMP intermediate and autoradiography, 576–577
  - base excision repair role, 253
  - blunt-end joining, 576
  - energetics, 575
  - pyridoxal phosphate inhibition, 575
  - viruses, 584
  - yeast, 582, 884
- DNA ligase I
- DNA repair, 580
  - human gene, 581
  - lagging strand ligation, 26, 580
  - mutants, 581–582
  - role in SV40 replication, 661
  - structure, 580–581
  - yeast enzyme, 582
- DNA ligase II, function, 583
- DNA ligase III
- functions, 583–584
  - XRCC1 protein binding, 583–584
- DNA ligase IV, immunolocalization, 584
- DNA polymerase. *See individual DNA polymerases; individual organisms; Processivity; Reverse transcriptase*
- classification, 468
  - gene expression, 476–478
  - structural conservation, 468–472
  - viral polymerases
    - regulation of expression, 513–516
    - sequence homology, 495
    - subunits, 496–497
- DNA polymerase I. *See* Klenow polymerase
- DNA polymerase III, subunits, 525–526
- DNA polymerase- $\alpha$ :primase
- accessory proteins, 158
  - associated helicase, 557, 562
  - catalytic mechanism, 466–467
  - DNA repair, 482
  - error rate, 222–225, 230, 239
  - exonucleolytic proofreading, 224

- DNA polymerase- $\alpha$ :primase (*continued*)  
 expression in cell cycle, 307, 476  
 general properties, 461–464  
 inhibitors, 157  
 phosphorylation, 307–310  
 primer synthesis, 3, 24, 45, 157–158, 446  
 protein interactions in polyomavirus replication, 652–653  
 recognition sites, 158–159, 446–447  
 role in DNA replication, 480–481, 651–653  
 site-directed mutagenesis, 224–225  
 structure-function relationships  
   active site, 469–470  
   dNTP-binding site, 471–473  
   metal binding, 470–472  
   primer-binding site, 471–474  
 subunits, 157, 307, 464–465, 651  
 switching genes in yeast, 478–479
- DNA polymerase- $\beta$   
 accessory proteins, 225  
 catalytic mechanism, 466–467, 474–475  
 DNA repair, 482–484  
 domains, 465, 474  
 error rate, 222, 225–226, 230, 239  
 gene expression, 476–477  
 general properties, 461–464  
 kinetoplast, 1038–1039  
 structure, 226, 474–475  
 structure-function relationships  
   catalytic triad, 474  
   metal binding, 175
- DNA polymerase- $\delta$   
 associated helicase, 562  
 auxiliary proteins, 24–25, 29, 226, 467, 658  
 DNA repair, 482–483  
 error rate, 222, 226, 230, 239  
 exonuclease, 658  
 gene expression, 477  
 general properties, 461–464  
 phosphorylation, 314  
 role in DNA replication, 481–482, 657–658  
 strand elongation, 5, 17  
 subunits, 314, 465, 657
- DNA polymerase- $\gamma$   
 catalytic mechanism, 467–468  
 error rate, 222, 226–227, 230, 239  
 exonucleolytic proofreading, 226, 1020  
 general properties, 461–463  
 mitochondrial localization, 461, 1020  
   subunits, 466, 1020–1021
- DNA polymerase- $\epsilon$   
 associated helicase, 562  
 auxiliary proteins, 24–25, 467, 659  
 DNA repair, 482–483  
 error rate, 222, 226, 230, 239  
 exonuclease activity, 658–659  
 exonucleolytic proofreading, 226  
 general properties, 461–464  
 phosphorylation, 314  
 role in DNA replication, 481  
 S-phase checkpoint role, 25  
 strand elongation, 5  
 subunits, 314, 465–466, 658–659  
 yeast mutants, 479
- DNA repair. *See* Base excision repair; Mismatch repair; Nucleotide excision repair
- DNA replication  
 common steps in mechanisms  
   opening at origins, 1–2  
   priming of synthesis, 2–4  
   strand elongation, 4–5  
   strand maturation, 5–6  
   unwinding at replication forks, 2  
 continuous replication, 3, 6  
 discontinuous replication. *See* Okazaki fragment  
 factories in nuclei, 121–123  
 fidelity. *See* DNA polymerases; Mismatch repair  
 linear genomes, 133–134, 140–141  
 mammalian initiators, 987–989  
 nuclear structure importance, 69–72, 120–121  
 semidiscontinuous replication  
   chromosomal DNA, 18–20  
   proofreading, 31, 217  
   protein-protein interactions, 27–30  
   replication centers, 31–32  
   replication fork enzymes, 21–27  
   viruses, 20–21  
 termination  
   eukaryotes, 177–179, 203–207, 454–455  
   prokaryotes, 177–181, 183–188, 190–202, 454
- DNA telomerase. *See* Telomerase
- DNA topoisomerase. *See* Topoisomerase
- D5 NTPase. *See* Vaccinia virus
- Drosophila*  
 chorion gene amplification, 427–428, 955–956, 960

- developmental alteration of replication, 410–411, 414–420, 422–428
- endo cell cycle, 423–425
- rDNA
  - amplification, 953–954
  - underrepresentation during polytenization, 952–953
- replication
  - bidirectional replicons, 947–949
  - cell-free replication system, 120
  - differential replication, 947, 950–951
  - inhibition in egg, 414–415
  - initiation regulation, 949–950
  - onion skin model and rested replication fork, 951
  - origins, 947–950, 959–960
  - protein requirements, 948–949
  - rapid embryonic cycles, 416–420, 948
  - replication fork
    - clustering, 123
    - rate of movement, 948
  - restart at egg fertilization, 415–416
  - satellite DNA in polytene chromosomes, 952, 958
  - underrepresented sequences, 951–957
- E1
  - DNA-binding mechanism, 688
  - helicase activity, 552–553
  - homology with T antigen, 680–681
  - initiation of replication, 442, 552–553, 686
  - origin-binding site, 685–686
  - origin recognition, 690–691
  - phosphorylation role in papillomavirus replication, 304
- E2
  - DNA-binding mechanism, 687–688
  - E1 binding, 100–101, 689–690
  - origin-binding sites, 685
  - origin recognition, 690–691
  - in papillomavirus replication, 688–690
  - stimulation of papillomavirus replication, 100–101, 687
- EBNA1
  - associated activities
    - ATPase, 758
    - helicase, 758
  - dimerization, 759
  - Epstein-Barr virus replication role, 751, 753–756, 759
  - plasmid maintenance role, 752–753, 757–758
  - structure, 759
- EBV. *See* Epstein-Barr virus
- Embryogenesis, replication changes
  - addition of G<sub>1</sub> in *Drosophila*, 422–423
  - gene amplification, 427–428
  - inhibition of replication in oocyte, 414–415
  - MBT in *Xenopus*, 421–422
  - mice, 420–421
  - polyploidy regulation, 423–427
  - posttranscriptional control, 417–418
  - regulation of entry into S phase, 411–412
  - replication origin control, 412–413, 418–419
  - restart of S phase at fertilization, 415–417
  - slowdown of S phase, 419–420
- Epstein-Barr virus (EBV). *See also* Herpesvirus
  - DNA polymerase
    - mapping of domain activities, 508
    - regulation, 514
    - structure, 506–507
  - DNA replication
    - arrest sites, 203
    - EBNA1 role, 751, 753–756, 759
    - initiation away from *oriP*, 759–761
    - initiation regulation, 757, 767–768
    - origins, 56–57, 103–104
      - oriLyt*, 763–767
      - oriP*, 751–756, 761–762
    - pausing, 756
    - termination, 756
    - transcription factor stimulation, 102–104
    - Z transcriptional activator, 763, 765–768
  - latency, 751
  - plasmid maintenance, 752–753, 757–758
- Erythrocyte, growth and cell cycle, 336
- Exonuclease
  - effect on fidelity of replication, 233–236, 239
  - proofreading, 220–222
- FEN-1
  - base excision repair role, 253
  - exonuclease processing of Okazaki fragments, 25
  - role in SV40 replication, 661
  - yeast, 883–884

- Fertilization, restart of S phase, 415–416
- Frameshift  
 error rates of DNA polymerases, 230  
 initiation mechanisms  
 misinsertion, 229  
 template-primer slippage, 227–228  
 processivity effects, 230–231
- G<sub>1</sub>  
 addition in *Drosophila* embryogenesis, 422–423  
 coordinating DNA replication and cell growth, 331–332  
 cyclin-dependent kinases  
 arrest with inhibitors, 333, 354–355  
 regulation, 346, 352–354, 360–362, 374, 409  
 late transcription  
 E2F activation, 356–357  
 factors, 344, 355–356  
 genes, 355  
 rationale for arrest, 374
- G<sub>2</sub>, DNA replication  
 cyclin-dependent kinase role, 360–362  
 licensing factor, 362–363  
 prevention of rereplication, 367–369
- Ganciclovir, drug resistance mutations, 507–508
- Geminivirus  
 agricultural threat, 833  
 DNA replication  
 origin  
 minus strand, 848–849  
 plus strand, 846–848  
 role  
 AL1, 837–842, 846–847  
 AL2, 843–844  
 AL3, 843  
 R2, 844–845  
 rolling circle model, 836–837  
 genomes, 834–836  
 subgroups, 834–835
- HeLa cell, effects on replication fidelity  
 in extracts  
 damaged substrates, 236–238  
 exonucleolytic proofreading, 233–236  
 mismatch repair, 232–233
- Helicase  
 accessory proteins, 566–567  
 assays, 545–547  
 DNA-binding protein inhibition, 565–566  
 DNA/RNA helicase superfamily, 547  
 eukaryotes, 445, 545, 556–561  
 loading in prokaryotes, 444–445  
 mechanism  
 creeping model, 565  
 rolling model, 563, 565  
 mitochondria, 17, 563  
 polarity, 2, 22, 546–547  
 structural motifs, 547–548  
 viral helicases. *See individual viruses*  
 yeast, 884
- Hepadnavirus  
 cytoplasmic core particle DNA, formation and amplification, 822–823, 826  
 DNA replication  
 protein priming of minus-strand synthesis, 143, 818–820, 824  
 reverse transcription, 143, 815–818  
 RNA packaging, 817–818  
 RNA priming of plus-strand synthesis, 820–822  
 hepatocyte infection, 815  
 reverse transcriptase  
 accessory proteins, 824–825  
 activities, 823–825  
 gene, 823  
 strains, 815  
 Hepatitis B virus. *See* Hepadnavirus
- Herpes simplex virus (HSV)  
 DNA polymerase  
 acyclovir sensitivity, 498  
 conserved regions, 501  
 drug resistance mutations, 501, 504–505  
 exonuclease activity, 500, 735  
 general properties, 498–499  
 processivity, 500, 735–736  
 subunits, 498, 734–735  
 translational shutoff, 514  
 UL42 interaction, 500, 735–736  
 homologous recombination and branched DNA structures, 722–723  
 ICP-8 single-stranded DNA-binding protein, 536, 734, 737–738  
 origins, 724–728, 765  
 UL5/UL8/UL52  
 helicase activity, 553–554, 738–739  
 primase activity, 553, 738–739  
 protein complexes, 554, 566  
 structure, 553

- UL9  
   ATPase activity, 731  
   dimerization, 731–732  
   helicase activity, 554–555, 724, 731, 733–734  
   origin binding, 554, 723, 726–727, 732–733, 763  
   polymerase interaction, 730  
   protein recruitment, 734  
   structure, 731  
 UL proteins and replication, 729, 734, 737–740
- Herpesvirus. *See also* Cytomegalovirus; Epstein-Barr virus; Herpes simplex virus
- DNA replication  
   DNA primase, 160–161  
   homologous recombination and branched structures, 722  
   origins, 723–724  
   rolling-circle model, 722  
   transcription factor stimulation, 102–104  
   genomes, 721  
   latency, 721  
   types, 496, 498
- Histone. *See* Chromatin
- HIV. *See* Human immunodeficiency virus
- hr* sequence. *See* Baculovirus
- HSSB. *See* Human single-stranded DNA-binding protein
- HSV. *See* Herpes simplex virus
- Human immunodeficiency virus (HIV)  
   minus-strand priming, 147  
   reverse transcriptase  
     closed conformation, 219  
     discrimination against base mispairs, 218–219  
     processivity and frameshift fidelity, 230–231  
   RNA secondary structure and minus-strand DNA synthesis, 149
- Human single-stranded DNA-binding protein (HSSB). *See* Replication protein A
- ICP-8. *See* Herpes simplex virus
- Imprinted genes, replication timing, 397–400
- Initiator RNA (iRNA)  
   length, 156, 160  
   Okazaki fragment priming, 153–154  
   radiolabeling, 154–156  
   site specificity for priming, 156–157
- Insect. *See also* *Drosophila*; *Sciara* puff chromosomes, 947
- DNA replication  
   bidirectional replicons, 947–949  
   differential replication, 947, 950–951  
   initiation regulation, 949–950  
   satellite DNA in polytene chromosomes, 952  
   underrepresented sequences, 951–960
- intrachromosomal amplification, 954–958
- rDNA  
   amplification, 953–954  
   underrepresentation during polytenization, 952–953
- iRNA. *See* Initiator RNA
- Kinetoplast  
   DNA  
     replication  
       cell cycle control, 1031–1032  
       DNA-binding proteins, 1039–1040  
       DNA polymerase  $\beta$ , 1038–1039  
       maxicircles, 1029, 1038  
       minicircles, 1029, 1037–1038  
       network replication problems, 1032  
       network structure, 1033–1035  
       protein complexes, 1032  
       spinning kinetoplast model, 1035–1036, 1040  
       termination, 1036–1037  
       topoisomerases, 1039  
       structure in *Crithidia fasciculata*, 1030–1031  
     parasitic species of Kinetoplastida, 1029
- Klenow polymerase  
   conformational change, 220  
   discrimination against base mispairs, 218–219
- Klenow polymerase (*continued*)  
   exonucleolytic proofreading, 220–222
- Licensing. *See* Replication licensing
- Linear DNA, protein priming of DNA  
   replication  
     chromosomes, 141  
     plasmids, 140–141
- Maturation factor I (MFN-I). *See* FEN-1
- MBT. *See* *Xenopus*

- MCM proteins. *See* Minichromosome maintenance proteins
- O*<sup>6</sup>-Methylguanine-DNA methyltransferase, mismatch repair, 263
- MFN-I. *See* Maturation factor I
- Minichromosome maintenance (MCM) proteins  
 nuclear membrane translocation, 127–128, 897  
 phosphorylation, 306–307  
 replication licensing, 126–128, 306  
 sequence analysis, 896–897  
 yeast genes, 896
- Minute virus of mice (MVM). *See also* Parvovirus
- DNA replication  
 origin  
 hairpin resolution, 807–808  
 junction resolution, 808–810  
 required proteins, 808  
 rolling hairpin model, 3, 7, 9, 800–802  
 genome, 805–806  
 life cycle, 799
- NS1  
 ATPase, 805  
 DNA binding, 805, 808  
 helicase, 556, 805  
 initiator endonuclease activity, 806  
 oligomerization, 806
- Mismatch repair  
 contribution to replication fidelity, 232–233, 239  
 defective cell tolerance to methylating agents, 263  
 inactivation and hereditary nonpolyposis colon cancer, 261–263  
 mechanisms of mismatch formation, 260  
 polymerases, 482–484  
 prokaryotes, 261  
 yeast, 261
- Mitochondria  
 displacement loop, 1015–1016  
 DNA deletion and disease, 1025  
 DNA replication  
 arrest sites, 204–205  
 chain elongation, 17–18, 1018–1019  
 continuous mechanism, 13–14  
 DNA polymerase- $\gamma$ , 461, 1020–1021  
 helicases, 17, 563  
 initiation  
 heavy-strand synthesis, 1016–1017  
 light-strand synthesis, 1017–1018  
 mammals, 1016–1022  
 priming, 14, 16, 152  
 regulation, 1021–1022  
 RNA-DNA hybrids, 1022  
 RNA processing for replication, 1019–1020  
 strand origins, 14, 16  
 yeast, 1022–1023  
 genome, 13, 1015–1016
- MPF. *See* M-phase promoting factors
- M-phase promoting factors  
 cell fusion studies, 337–338  
 Clb cyclins in yeast, 341–343  
 cyclin-dependent kinases, 360–361  
 M-phase promoting factor, 337–338, 344–345, 372
- MVM. *See* Minute virus of mice
- N-2-Acetylaminofluorene adduct, effect on replication fidelity, 238
- NFI. *See* Nuclear factor 1
- Nuclear factor 1 (NFI)  
 DNA-binding specificity, 91–92  
 domains, 91  
 stimulation of adenovirus replication  
 initiation, 91–92, 142, 701–702, 708–710
- Nuclear scaffold  
 mammals, 984  
 nuclear structure role in initiation of metazoan replication, 69–72
- Nucleosome. *See* Chromatin
- Nucleotide excision repair  
 comparison with RNA polymerase II transcription initiation, 255, 257  
 defects in xeroderma pigmentosum, 255  
 human repair genes, 255–256  
 proteins  
 DNA-binding proteins, 259  
 DNA helicases, 259  
 endonucleases, 257–259  
 polymerases, 482–484  
 replication protein A, 260  
 TFIIH role, 255, 257–258
- Oct-1. *See* Octamer-binding transcription factor 1
- Octamer-binding transcription factor 1 (Oct-1)  
 DNA-binding specificity, 93

- stimulation of adenovirus replication
  - initiation, 93–94, 142, 701–702, 710–711
- Okazaki fragment
  - length, 153
  - processing, 18, 25, 665
  - synthesis
    - cycling of pol- $\alpha$ :primase, 30–31
    - initiation, 152–153
    - initiation zone model, 161–162
    - nested discontinuity model, 162–163
    - polyomavirus, 663–664
    - primer. *See* Initiator RNA
- Onion skin model. *See Drosophila*
- ORC. *See* Origin recognition complex
- OriC*
  - Escherichia coli* replicator, 439
  - initiation control, 453–454
- Origin. *See also organisms*
  - classification, 47
  - complex (metazoan) origins
    - amplification promoting element, 67
    - autonomously replicating sequences, 57, 65–66
    - chromosome mapping, 57, 59–61, 63
    - densely methylated island, 68
    - DNA-unwinding element, 67–68
    - heredity, 64–65
    - initiation zone, 61, 63, 66, 73–75
    - models for replication
      - Jesuit model, 73–76
      - migrating replication complex model, 73
      - strand separation model, 72–73
    - nuclear scaffold attachment sites, 68–69
    - nuclear structure role in initiation of replication, 69–72
    - origin of bidirectional replication, 59, 61–64, 73
    - palindromic sequences, 68–69
    - quiet zone, 75
    - replication complex, 75–76
    - transcription-factor-binding sites, 67
  - distribution in genome, 46–48, 437
  - mammals, identification, 986–988, 991–993
  - meiotic origins
    - spatial control, 412–413
    - temporal control, 413
  - mitochondria, 14, 16
  - opening of DNA, 1–2, 45, 441
  - simple genome origins
    - A/T-rich element, 54
    - autonomously replicating sequences, 50, 412
    - auxiliary components, 54–56
    - DNA-unwinding element, 53–54
    - genetic versus functional origin, 50
    - origin core, 49
    - origin recognition element, 51
    - origin recognition proteins, 51–52
    - transcription factors
      - binding sites, 49–50
      - stimulation of origin core, 55–56
    - viruses, 56–57, 104
    - yeast. *See* Origin recognition complex
  - Origin recognition complex (ORC)
    - components, 305, 890
    - footprinting, 105, 305, 890
    - phosphorylation, 305–306
    - replication initiation, 32, 286, 890, 986
    - repression of transcription, 282–283, 890–891
    - sequence recognition, 105, 305
    - transcription factor stimulation, 105–107
  - oriP*. *See* Epstein-Barr virus
  - 8-Oxo-deoxyguanosine, effect on replication fidelity, 237
  - Papillomavirus. *See also* E1; E2
    - DNA replication
      - assays
        - cell-free replication, 682
        - long-term assays, 681
        - short-term assays, 682
      - bovine virus in tissue culture, 679–680
      - origin, 100, 683–686
      - required proteins, 99–100
      - requirements, in vitro, 687
      - transcription factor stimulation, 100–101
    - life cycle, 679
    - maintenance, 691–692
  - Papovavirus. *See* Papillomavirus; Polyomavirus; SV40
  - PARP. *See* Poly(ADP-ribose) polymerase
  - Parvovirus. *See also* Adeno-associated viruses; Minute virus of mice
    - classes, 7
    - DNA replication
      - concatemeric duplex intermediates, 800–801
      - origin, 56–57
      - rep* gene requirement, 6

- Parvovirus (*continued*)  
 rolling hairpin model, 3, 7, 9, 800–802, 810–811  
 genome, 799
- Pause site  
 biological roles, 179–180  
 sequences, 177–179
- PCNA. *See* Proliferating cell nuclear antigen
- PCR. *See* Polymerase chain reaction
- Phage Cp-1, protein priming of DNA replication, 140
- Phage  $\phi$ 29, DNA replication  
 fidelity, 144  
 ion stimulation, 135  
 origin, 137  
 pause sites, 179  
 polymerase-terminal protein interactions, 136–137  
 requirements for initiation, 134–136  
 sliding-back mechanism for transition from initiation to elongation, 143–146  
 stimulating proteins  
 p5, 138–139  
 p6, 137–138  
 terminal protein priming, 132–133
- Phage PRD1  
 protein priming of DNA replication, 139  
 sliding-back mechanism for transition from initiation to elongation, 144–145
- Physarum*  
 DNA replication  
 chromosomal origins, 941, 943–944  
 DNA bubbles, 937  
 kinetics, 935, 937  
 rDNA, 941–942  
 replicon  
 clustering, 938  
 structure, 935–937  
 timing  
 effect on gene expression, 939  
 programming, 938–939  
 plasmodium development, 933  
 synchrony of nuclear cycle, 933, 935
- p16INK4, G<sub>1</sub> arrest, 354
- Plants  
 chromosomal DNA maturation, 1007–1008  
 genomic diversity, 1005  
 origin number, factors affecting, 1007
- rDNA  
 clustering, 1009  
 intergenic spacer region organization, 1009  
 replication mechanisms in pea, 1010–1012
- replicon  
 clusters, 1008  
 families and S-phase duration, 1006  
 fork rate, 1006–1007  
 size, 1006–1007
- Plasmodium. *See* *Physarum*
- Poly(ADP-ribose) polymerase (PARP), base excision repair role, 254
- Polymerase chain reaction (PCR), chromosome mapping, origins of replication, 59
- Polyomavirus. *See also* SV40  
 DNA replication  
 auxiliary elements, 643–644  
 elongation, 664–665  
 lagging strand synthesis, 663–664  
 leading strand synthesis, 663  
 maturation of Okazaki fragments, 665  
*ori*-core, 642  
 origin, 640, 642–644  
 polymerases, 650–653, 657–659  
 presynthesis, 662  
 primosome assembly, 662  
 proliferating cell nuclear antigen role, 653–655  
 replication factor C role, 655–657  
 replication protein A role, 648–651  
 species specificity, 651–652  
 termination, 667  
 topoisomerases, 659–680  
 transcriptional activators, 644
- T antigen  
 binding specificity, 645–646  
 helicase activity, 552, 640, 647  
 phosphorylation role in replication, 303–304, 646–647  
 protein-protein interactions, 646, 650–651  
 structure, 644–645  
 transcription factor stimulation of replication, 98–99
- Polyteny  
 endo cell cycle regulation, 424–426  
 heterochromatin underrepresentation, 426–427  
 S-phase regulation in embryogenesis, 423–424

- Poxvirus. *See also* Vaccinia virus
- DNA replication
    - concatemeric intermediates, 777
    - consensus resolution sequence, 784
    - cytoplasmic localization, 776
    - DNA repair link, 791–793
    - leading strand synthesis, 781
    - proteins, 785–791
    - rate, 776–777
    - resolution of intermediates, 783–785
    - sequences required for replication, 782–783
    - strand cleavage, 781
    - ts* mutants, 785
  - life cycle, 775–776
- Primase. *See* DNA polymerase- $\alpha$ :primase
- Primer
- mitochondria, 147–150, 152
  - Okazaki fragment. *See* Initiator RNA
  - prokaryotes, 446–447
  - protein primer for virus DNA replication
    - adenovirus, 3, 141–142
    - hepadnavirus, 143
    - linear chromosomes, 141
    - linear plasmids, 140–141
    - phage Cp-1, 140
    - phage  $\phi$ 29, 132–139
    - phage PRD1, 139
  - removal from DNA strands, 5
  - RNA-DNA primer synthesis, 159–160
  - synthesis. *See* DNA polymerase- $\alpha$ :primase
  - transfer RNA primer encapsidation by retroviruses, 146–147
  - types, 131–132
- Processivity
- accessory protein role, 526
  - effect on frameshift fidelity, 230–231
  - telomerases, 632
- Proliferating cell nuclear antigen (PCNA)
- binding to DNA polymerase, 5, 24–25, 29, 449–450, 528–529, 654
  - cell cycle regulation, 529–530, 655
  - crystal structure, 654
  - detection at replication centers, 31–32
  - discovery, 526
  - DNA loading, 529, 531, 533–534
  - DNA-repair role, 450, 654–655
  - genes, 528
  - half-life, 654
  - homology with DNA polymerase III, 19
  - phosphorylation, 33, 314–315
  - physical properties, 528
  - primer recognition complex, 529
  - yeast, 880–881
- R2. *See* Geminivirus
- Rb. *See* Retinoblastoma protein
- rDNA. *See* Ribosomal gene
- Rep proteins. *See* AL1; Adeno-associated viruses
- Replication factor C (RF-C)
- associated helicase, 557
  - ATPase activity, 530, 656
  - discovery, 526, 530
  - DNA footprinting studies, 530
  - effects on DNA polymerases, 530–531, 656–657
  - loading of proliferating cell nuclear antigen on DNA, 529, 531, 533–534, 656
  - phosphorylation, 314–315
  - subunits, 531, 655–657
  - yeast, 881–882
- Replication foci, assembly in mammals, 984–985
- Replication fork
- arrest at replication termini in prokaryotes. *See also* Replication terminator protein; Ter
    - activation under stringent conditions, 197–198
    - chromosomal location of arrest sequences, 184
    - detection of termini, 180–181, 183–184
    - physiological roles, 198–199
    - structure of arrest sequences, 184–186
  - clustering in nucleus, 121–123
  - mammals, 987–988
  - pause sites
    - biological roles, 179–180
    - sequences, 177–179
  - polarity, 60
  - rate of movement, 19–20, 387–388, 436, 948, 1006–1007
  - transcription factor displacement, 278
- Replication licensing
- licensing factor
    - components, 976
    - S-phase control, 362–363, 974–978
  - nuclear structure role, 125–128, 286–287
  - one-time initiation during cell cycle, 77, 119, 123, 125

- Replication licensing (*continued*)  
 rereplication  
   cyclin-dependent kinase prevention, 367–369  
   yeast mutants, 366–367
- Replication origin. *See* Origin
- Replication protein A (RP-A)  
 activities, 534–535  
 associated helicase, 562  
 detection at replication centers, 31–32  
 discovery, 526, 534  
 DNA binding in replication, 23–24, 45, 310–311  
 DNA recombination role, 311  
 phosphorylation, 33, 312–314, 535–536, 650  
 protein interactions in SV40 replication, 28–30, 96–97, 648–651  
 role in nucleotide excision repair, 260  
 subunits, 23, 534–535, 648–649  
 yeast, 882
- Replication terminator protein (RTP)  
 helicase inhibition, 190–192, 207  
 purification, 186  
 replication arrest site interaction, 191  
 structure  
   crystal structure, 192–193  
   dimer-dimer interaction domain, 194–196  
   dimerization domain, 194  
   DNA-binding domain, 193–194  
   helicase-blocking surface, 196–197  
   subunits, 191
- Replication terminus  
 eukaryotes  
   arrest sites, 203–205  
   sibling molecule separation at termination sites, 205–207  
 prokaryotes  
   activation under stringent conditions, 197–198  
   chromosomal location, 184  
   detection of termini, 180–181, 183–184  
   physiological roles, 198–199  
   recombination activity, 202  
   structure, 184–186
- Replication timing  
 assay, 388, 392–393  
 effect on gene expression  
   chromatin structure role, 403  
   developmental changes, 390  
   housekeeping genes, 388–390  
   imprinted genes, 397–400  
   mechanism in *Xenopus*, 401–403  
   prokaryotes, 387  
   X chromosome, 395–397, 399–400  
   yeast, 388, 403  
 genome reproduction time, 19–20, 387–388  
 prokaryotes, 387  
 regulation  
   allelic exclusion, 400–401  
   *cis*-acting elements, 394–395  
   locus control region, 395–396  
   methylation of DNA, 397–398  
   regional regulation, 398–400  
   telomere, 395  
 replicon structure, 393–394  
 time zones in mammalian cells, 390, 392–393, 401, 404
- Replicon  
 clustering, 938, 984, 1008  
*Drosophila*, 123, 947–949  
 mammals, 983–985  
*Physarum*, 935–938  
 plants, 1006–1008  
 replication timing, 393–394
- Retinoblastoma protein (Rb)  
 cell cycle regulation, 356–357  
 cyclin regulation, 358  
 E2F association, 356  
 phosphorylation, 356, 409
- Retrotransposon  
 primer-binding site, 150, 152  
 reverse transcription initiation, 150–152
- Retrovirus. *See also* Human immunodeficiency virus  
 minus-strand priming, 147  
 plus-strand priming, 149–150  
 RNA secondary structure and minus-strand DNA synthesis, 147–149  
 transfer RNA primer encapsidation by retroviruses, 146–147
- Reverse transcriptase. *See* Human immunodeficiency virus
- RF-C. *See* Replication factor C
- Ribonuclease H  
 primer removal from DNA strands, 5  
 role in SV40 replication, 660
- Ribonuclease MRP, mitochondrial RNA processing for replication, 1019–1020
- Ribosomal gene (rDNA). *See Drosophila; Physarum; Plants; Tetrahymena*

- Ribosomal RNA (rRNA), replication arrest sites in yeast genes, 203–204
- RP-A. *See* Replication protein A
- rRNA. *See* Ribosomal RNA
- RTP. *See* Replication terminator protein
- Saccharomyces cerevisiae*. *See* Yeast
- Saccharomyces pombe*. *See* Yeast
- Sciara puff, developmental amplification, 428, 957–958, 960
- Single-stranded DNA-binding protein (SSB)
- adenovirus, 536
  - effect on polymerase fidelity, 231–232
  - herpes simplex virus, 536
  - role in SV40 replication, 23–24
- SPF. *See* S phase, promoting factors
- S phase
- checkpoint role of DNA polymerase- $\epsilon$ , 25
  - dependence on anaphase, 371–372
  - dependence on cell growth, 333–334
  - developmental meiosis
    - inhibition of replication in oocyte, 414–415
  - MBT in *Xenopus*, 421–422
  - mice, 420–421
  - polyploidy regulation, 423–427
  - posttranscriptional control, 417–418
  - regulation of entry into S phase, 411–412
  - replication origin control, 412–413, 418–419
  - restart of S phase at fertilization, 415–417
  - slowdown of S phase, 419–420
  - genetic analysis in animals, 359–360
  - initiation of replication, dependence on phase, 47–48, 77, 119
  - premeiotic S phase, 411–413
  - promoting factors
    - animal cells, 351–352
    - cell fusion studies, 337–338
    - mechanism of promotion, 348–349
    - S-phase promoting factor, 337, 344–345, 348, 372
  - Saccharomyces cerevisiae* factors
    - Cdc6, 365
    - Cdc7, 347–348
    - Cln cyclins, 340–344
    - cyclin-dependent kinases, 339–342, 345, 374–375, 409–410
    - G<sub>1</sub>-specific transcription factors, 344
    - genes, 338–339
    - meiosis control, 410–412
    - p40Sic1, 346–347
    - Saccharomyces pombe*, 350–351
    - rereplicating yeast mutants, 366–367
    - triggering by growth-related protein synthesis, 334–336
    - two-step mechanism for onset
      - chromatin structure during cell cycle, 364
      - feasibility, 372
      - licensing factor, 362–363
      - pre-RC formation, 365–366, 369–370, 373–374
      - yeast, 363–367
- SSB. *See* Single-stranded DNA-binding protein
- SV40
- DNA replication
    - auxiliary elements, 643–644
    - cell-free system, 20
    - DNA ligase, 26, 661
    - DNA polymerases, 24–25, 651–653, 657–659
    - elongation, 664–665
    - FEN-1, 661
    - lagging strand synthesis, 663–664
    - leading strand synthesis, 663
    - maturation of Okazaki fragments, 665
    - nucleases, 25
    - Okazaki fragment synthesis, 30–31
    - ori-core, 642
    - origin, 94–95, 640, 642–644
    - ori replicator, 439–440
    - pause sites, 179
    - presynthesis, 662
    - primase, 24, 651–653
    - primosome assembly, 662
    - proliferating cell nuclear antigen role, 653–655
    - protein phosphorylation role, 32–33, 297–300, 302–303, 646–647
    - protein–protein interactions, 27–30, 96, 650–651
    - replication factor C role, 655–657
    - replication protein A role, 648–651
    - replication proteins, 21–22, 296–297
    - ribonuclease H, 660
    - S-phase dependence, 296
    - single-stranded DNA-binding protein, 23–24

- SV40 (*continued*)  
 species specificity, 651–652  
 T antigen role, 297–300, 302–303, 550–552  
 termination, 667  
 topoisomerases, 26–27, 659–680  
 transcription factor stimulation, 95–98, 644  
 genome, 296  
 T antigen  
 binding specificity, 645–646  
 helicase  
 accessory proteins, 566  
 essential residues, 551–552  
 mechanism, 647  
 nucleotide specificity, 550  
 replication fork interactions, 550–551  
 protein–protein interactions, 646  
 structure, 644–645
- T antigen  
 binding specificity, 645–646  
 helicase activity  
 mechanism, 647  
 polyomavirus, 552  
 SV40, 550–552  
 initiation of replication, 442  
 phosphorylation state in DNA replication  
 analysis, 316–317  
 kinases, 302–303, 647  
 polyomavirus, 303–304, 646–647  
 SV40, 298–300, 302–303, 443, 646–647  
 protein–protein interactions, 646, 650, 652–653  
 structure, 644–645
- T4 DNA polymerase, discrimination  
 against base mispairs, 218–219
- T7 DNA polymerase  
 closed conformation, 219  
 discrimination against base mispairs, 218–219  
 processivity and frameshift fidelity, 231  
 thioredoxin role, 231
- Telomerase  
 activity in human cancers, 634–635  
 mammalian telomerase RNA  
 cloning, 626  
 human, 626  
 mouse, 626–627  
 nucleotide specificity, 630–631  
 processivity, 632  
 telomeric sequences, 619  
*Tetrahymena* enzyme  
 assays  
 gel-banding assay, 619–621  
 polymerase chain reaction, 622  
 primer binding, 629–630  
 reconstitution assay, 623–624  
 nucleotide specificity, 630–631  
 primer affinity, 628–630  
 protein structure, 632–633  
 RNA component  
 mutation studies, 627  
 secondary structure, 622–623  
 sequence, 622  
 template region, 623–624  
 yeast telomerase RNA  
 cloning, 625  
 mutation studies, 627–628  
 secondary structure, 625–626  
 telomere silencing role, 625
- Ter  
 helicase inhibition, 188, 190–191, 207  
 interaction with replication arrest sites, 187–188  
 regulation of synthesis, 198  
 structure, 186
- Terminal protein (TP)  
 deoxynucleotide complexes  
 dAMP, 135, 144  
 dCMP, 142, 145  
 dGMP, 139  
 DNA polymerase interactions, 136–137  
 precursor processing in adenovirus, 702–704  
 priming of DNA synthesis in viruses, 132–133, 702–704
- Termination. *See* Replication terminator protein; Replication terminus
- Tetrahymena*  
 minichromosome formation, 917–919  
 nuclei, 916  
 rDNA replication  
 cell cycle control, 915–916, 928  
 copy number control, 915–916, 928  
 DNA/protein interactions in origin region, 927–928  
 maintenance mutants, 924–925  
 monomers, 921  
 5' NTS importance, 925, 929  
 origin, 921–924  
 palindromes, 921  
 regulation of vegetative replication, 926

- transcriptional suppression, 926
- regulation of rDNA amplification, 919–921
- telomerase
  - assays
    - gel-banding assay, 619–621
    - polymerase chain reaction, 622
    - primer binding, 629–630
    - reconstitution assay, 623–624
  - nucleotide specificity, 630–631
  - primer affinity, 628–630
  - protein structure, 632–633
  - RNA component
    - mutation studies, 627
    - secondary structure, 622–623
    - sequence, 622
    - template region, 623–624
- TFIIH, role in nucleotide excision repair, 255, 257–258
- Timing. *See* Replication timing
- Topoisomerase
  - decatenation of daughter chromosomes
    - prokaryotes
      - multimer resolution, 202
      - topo II, 201
      - topo IV, 200
    - yeast, 603
  - inhibitors
    - classification, 597, 600
    - cytotoxicity, 600–601
    - mechanisms of inhibition, 600
    - table, 598–599
  - kinetoplast, 1039, 882–883
  - meiosis role, 603
  - phosphorylation, 315–316
  - prokaryotes, 451–452
  - protein interactions, 605
  - recombination role, 603–604
  - role in SV40 replication, 26–27, 602–603, 659–660
  - transcription modulation, 601–602
  - type I
    - catalytic activity, 26, 587–588
    - functions, 601–603
    - genes, 659–660
    - mechanism of strand passage, 592
    - structure, 588
    - substrate specificity, 590, 592
  - type II
    - catalytic activity, 26, 587, 594–597
    - functions, 602–603
    - human gene expression, 593–594, 660
    - mechanism, 595–597
    - phosphorylation, 594
    - structure, 592–593
    - types, 26, 587, 659
- TP. *See* Terminal protein
- Transcription factors. *See also individual transcription factors*
  - binding sites
    - complex origin, 67
    - simple genome origin, 49–50
    - viruses, 87
  - enhancement of replication
    - adenovirus, 91–94
    - comparison with transcriptional activation, 109–110
    - herpesvirus, 102–104
    - mechanisms, 88–89
    - papillomavirus, 99–101
    - polyomavirus, 98–99
    - rational, 107–109
    - stimulation origin core, 55–56
    - SV40, 94–98
    - yeast, 104–107
- Transfer RNA (tRNA), primer encapsidation by retroviruses, 146–147
- tRNA. *See* Transfer RNA
- Two-dimensional gel electrophoresis
  - chromosome mapping, origins of replication, 60–61, 63–64
  - replication termini in prokaryotes, detection, 183–184
- UL proteins. *See* Herpes simplex virus
- Ultraviolet damage, effect on replication fidelity, 237–238
- Vaccinia virus
  - B1 protein kinase, 788
  - D5 NTPase, 787–788
  - DNA-binding protein, 791
  - dUTPase, 792
  - helicase, 791
  - nucleoprotein complex, 778–779, 781
  - ribonucleotide reductase, 790
  - telomeric sequence organization, 777–778
  - thymidine kinase, 789–790
  - topoisomerase I, 790–791
  - uracil DNA glycosylase, 792–793
  - DNA ligase, 584–585, 789
  - DNA polymerase
    - accessory proteins, 510, 787
    - drug-resistant mutants, 510

- DNA polymerase (*continued*)  
 drug sensitivity, 509–510, 787  
 exonuclease, 509, 786  
 processivity, 787  
 regulation, 515  
 structure, 509, 785
- DNA replication  
 concatemeric intermediates, 777  
 consensus resolution sequence, 784  
 cytoplasmic localization, 776  
 DNA-repair link, 791–793  
 leading-strand synthesis, 781  
 rate, 776–777  
 resolution of intermediates, 783–785  
 sequences required for replication, 782–783  
 strand cleavage, 781  
*ts* mutants, 785
- X chromosome, replication timing, 395–397, 399–400
- Xenopus*  
 cell cycle control, 362–363, 974–976  
 chromatin assembly, 279–280  
 cyclin-dependent kinases, 977–978  
 DNA replication  
 cell-free replication system, 120, 971  
 developmental alteration of replication, 410–411, 414, 416–422  
 initiation, 972–974, 977–978  
 licensing factor control, 362–363, 974–976  
 nuclear assembly role, 971–973  
 origins, 973  
 polymerase, 972  
 proliferating cell nuclear antigen, 972  
 replication fork clustering, 123  
 MBT, 421–422  
 S-phase promoting factor, 977–978  
 XRCC1. *See* DNA ligase III
- Yeast  
 chromatin transcriptional states, 282–286  
 cyclin-dependent kinases  
 replication control, 893–896  
 rereplication prevention, 367–369  
 DNA replication. *See also* Origin recognition complex
- autonomously replicating sequences  
 binding proteins, 887, 889–892  
 identification, 873, 985–986  
 structure, 885–889
- DNA ligase, 582, 884  
 enhancement by transcription factors, 104–107
- FEN-1 homolog, 883–884  
 helicase, 884  
 MCM proteins, 896–897  
 origins  
 chromosomal, 889  
 determinants of use, 897–900  
 origin interference, 898–899  
 polymerases, 874–875, 880  
 proliferating cell nuclear antigen, 880–881  
 replication factor C, 881–882  
 replication fork proteins, table, 876–879  
 replication protein A, 882  
 termination, 902–903  
 timing  
 control, 901–902  
 gene expression effects, 388, 403  
 topoisomerases, 882–883  
 mismatch repair, 261  
 polymerase switching, 478–479
- S-phase onset  
 mechanism, 363–367
- Saccharomyces cerevisiae* factors  
 Cdc6, 365  
 Cdc7, 347–348, 893–894  
 Cln cyclins, 340–344  
 cyclin-dependent kinases, 339–342, 345, 374–375, 409–410  
 G<sub>1</sub>-specific transcription factors, 344  
 genes, 338–339  
 meiosis control, 410–412  
 p40Sic1, 346–347
- Saccharomyces pombe* factors, 350–351
- telomerase RNA  
 cloning, 625  
 mutation studies, 627–628  
 secondary structure, 625–626  
 telomere silencing role, 625
- Z. *See* Epstein-Barr virus