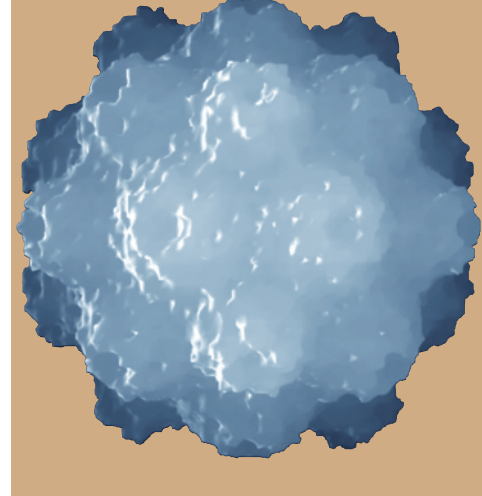


# Index



*Note:* page numbers in *italics* refer to figures; those in **bold** to tables.

- Abelson murine leukemia virus **393**
- abortive infections 160–1
- acetylcholine receptor 23, **82**, **82**
- acid blob activator 343
- acquired immune deficiency syndrome *see* AIDS
- acute infections 24–5, 44
- dynamics in human populations 42
- history of association with humans 48–9
- patterns in humans 49–50, *51*
- viruses causing **45–7**
- acyclovir (acG) 132, *133*
- adaptive immunity 20, 98, 100–8
- adeno-associated virus (AAV) 323–5, *324*
- antivirus strains 493
- gene therapy vectors **452**, 453, **491**
- Adenoviridae **70**
- adenoviruses **29**, **45**, 319–23
- 72-kd DNA-binding protein (72KDBP) 320, 321
- capsid proteins 179, *180*
- capsid structure 180, 319
- cytopathology 321–3
- DNA replication 217, 321, 322
- evasion of immunity 111–12, 321–3
- gene therapy vectors **452**, 453, **491**
- genome 319, *320*
- helper virus function 324–5
- mRNA splicing 228–30, 319, 320, 321
- replication 304, 319–23
- VA RNA 319, 321–3
- adjuvants 125
- aerosols, infectious 27, 28
- African green monkey kidney cells (AGMK) 306
- agnoprotein 310, *311*, 312
- AIDS 6–7, 23, 399
- drug therapy 134–5
- emergence 485–6, *486*, 487, 488
- pandemic 399–400
- pathogenesis 408, 408–9
- see also* HIV
- alfalfa looper nuclear polyhedrosis virus (AcNPV) 355
- algal viruses 9, 20–1, 376
- aliquots 169
- All the Virology of the WWW **483**, 505
- Allexivirus* 70
- $\alpha$ -TIF protein 340, 341–3, *342*
- amantadine 133, 133–4
- ambisense genomes 290, *291*, 292
- amino acid sequences, similarity searching tools 476, *477*
- amino acid transporter, cationic **82**
- ampicillin resistance marker 445, 448–9
- aneuploid cells 158
- angiotensin converting enzyme 2 (ACE2) 265–6, 267
- animal cells 16
- culture 157, 157–60
- transformation 17
- virus entry 80–5, *81*
- animal models 34–40, 464–6
- applications 466–70
- humane use 465–6
- hybrid 464–5
- latent HSV infections 37–40, *39*
- natural host *vs.* surrogate 464
- poxvirus 35–7, *36*
- rabies 37, 38
- transgenic 464, *465*
- animals
- impact of viral infections 8
- reservoirs 28, 30
- role of viruses in evolution 9
- antibodies 100, *102*, 195–7
- detection of antigen-bound 201–4
- immunofluorescence methods 198–201, *199*
- measurement of antiviral 112–17, 470
- molecular structure 196, *197*
- monoclonal 196–7, *198*
- neutralizing 114, *115*
- polyclonal 196
- antigen-presenting cells (APC)
- 100, 104–6
- professional 106
- antigenic drift 110, 285
- antigenic shift 287
- antigens 24, 100
- detecting antibodies bound to 201–4
- presentation *104–5*, 104–6
- structure 102–4, *103*
- see also* proteins, viral
- antiretroviral therapy 134–5
- decay of HIV-1 viremia 409, 409–10
- highly active (HAART) 134–5
- antisense oligonucleotides 135
- antiserum 195–6
- monospecific 196

- antiviral drugs 131–5  
 combination use 134–5  
 precise targeting approach 135  
 targeting virus replication 131–5, **132**
- antiviral effector molecules (AVEMs) 128, 129
- antiviral state 128, 129
- apathogenic strain 5
- APOBEC proteins 131, 401–4, 404
- apoptosis  
 adenovirus-mediated stimulation 323  
 cultured cells 159  
 EBV-induced inhibition 352  
 HIV-induced 406  
 infected cells 128, 162, 162–3  
 SV40-induced inhibition 314  
 viral inhibition 164
- arabinosyl adenine 133
- arabinosyl cystosine 133
- arboviruses 56, 75–7, 263, 288
- archaeobacteria (Archaea) 10, 10
- Arenaviridae **70**
- arenaviruses 111, 291–2  
 pathogenesis 292  
 replication 291, 292
- Arteriviridae **70**
- arthropod vectors 30, 56, 263
- arthropod viruses 355–6
- ascites 198
- Ascoviridae **70**
- Asfarviridae **70**
- Astroviridae **70**
- atomic force microscopy 151–2, 152
- attenuation 121, 122–3
- AUG initiation codon 233, 235  
 poliovirus 251  
 skipping, SV40 virus 310
- Autographa californica* nuclear polyhedrosis virus (AcNPV) 355, 356
- autoimmune diseases 52–3, 109
- avian erythroblastosis virus **393**
- avian erythroblastosis virus-ES4 **393**
- avian influenza 8, 33, 48, 288
- avian leukosis virus (ALV) 386, 387
- avian myelocytoma virus **393**
- avian sarcoma virus **393**
- avirulent strain 5
- azidothymidine (AZT) 133, 134
- B lymphocytes 100, 102  
 antigen presentation 106  
 clonal selection 107, 107
- EBV infection 23, 351–4  
 effector 24  
 epitopes 102–3  
 immortalization 159–60, 352–3  
 maturation 107  
 memory 108  
 viruses infecting **22**
- Bacillus subtilis* 292
- bacteria  
 antiviral defenses 135–6  
 cell culture 156  
 cell structure 16  
 genome organization 214  
 plasmids, cloning using 444–9  
 restriction response 19, 135–6  
 transposons **395**, 395–6, 397  
*see also* prokaryotes
- bacterial artificial chromosomes (BACs) 444, 452, 458–60
- bacteriophages 7  
 cloning vectors 449–51  
 DNA injection into *E. coli* 87–9, 88  
 large DNA-containing 365–76  
 phylogenetic relations 376  
 replication 365–76  
 structure 365, 366  
 male specific 89  
 RNA-containing 269–71  
 ssDNA, replication 326, 327
- Baculoviridae **70**
- baculoviruses 232, 355–6  
 cloning/expression systems 356, 452, **452**  
 replication 356
- badnaviruses 416, 417
- Baltimore classification scheme 75
- barley yellow dwarf virus **268**
- Barnaviridae **70**
- Benyvirus* **70**
- $\beta$ -galactosidase (lacZ)  
 reporter protein 468, 468, 492, 492  
 screening marker 445, 451, 456–8
- betapropiolactone 123
- bioinformatics 473–81  
 applications 476–8  
 databases 474–6, 475  
 internet resources 481, **483**  
 systems biology approaches 479–81
- biological activity, measurement of viral 164–70
- biological control 36, 356
- biological weapons 489–90
- bioluminescent imaging (BLI) 468–9, 469
- biosphere 4, 9–10, 494
- biotechnology 356
- bioterrorism 8, 121, 364–5, 489–90
- Birnaviridae **70**
- BK virus **45**, 52, 308
- BLAST 476, 477
- blood–brain barrier 54–5
- bluetongue virus 295
- body fluids, transmission via 28
- books, reference 501–3
- Bornaviridae **70**, 275
- bornaviruses 282–3
- bovine immunodeficiency virus (BIV) 399
- bovine papillomavirus 316
- bovine spongiform encephalopathy (BSE) (mad cow disease) 13, 298, 299–300
- brome mosaic virus 85, **268**, 269
- Bromoviridae **70**
- BSE *see* bovine spongiform encephalopathy
- budded viruses (BVs) 355
- budding 94, 95
- Bunyaviridae **70**, 288
- Bunyavirus* **289**, 289–90
- bunyaviruses **47**, 288–91, **289**  
 ambisense genomes 290, 291  
 exit from cells 94  
 pathogenesis 291  
 structure and replication 288–90, 290
- buoyant density 174, 175
- Burkitt's lymphoma 354
- burst size 15
- C-proteases 251
- Cadang-Cadang viroid 8–9, **29**, 297
- calcium phosphate 89, 90
- Caliciviridae **70**
- cAMP *see* cyclic AMP
- cancer 52  
 hepatitis B virus-induced 416  
 herpesvirus-associated 354–5  
*see also* tumors
- canine distemper 281
- canine parvovirus 489
- cap-binding protein (CBP1) 233, 234
- cap site 221–2
- cap snatching (stealing) 284, 286, 289
- capillary electrophoresis, DNA sequencing 183, 184
- Capillovirus* **70**

- capping, mRNA 224–5, 227  
 negative-sense RNA viruses  
 276–7, 283, 285, 289, 292  
 plant RNA viruses 268, 269  
 positive-sense RNA viruses  
 257, 258, 259, 266, 267,  
**268**  
 RNA viruses with dsRNA  
 genomes 294  
 caprine arthritis-encephalitis virus  
 (CAEV) 399  
 capsid(s) 65, 69–72  
 assembly 89–93, 91, 92  
 atomic force microscopy 152  
 cryoelectron microscopy 149,  
 150  
 disruption 179, 181  
 formation 80  
 intracellular transport 85, 87  
 nanotechnology applications  
 493–4  
 proteins  
 pulse labeling studies 194,  
 195  
 stoichiometric analysis  
 177–9, 178, **179**, 180  
*see also* structural proteins  
 structure 72, 73, 74  
 vaccines 124–5  
 capsomers 69, 72  
*Carlavirus* **70**  
 catabolite repression 221  
 cauliflower mosaic virus 416–17,  
 417  
 Caulimoviridae **70**  
 caulimoviruses 416, 417  
 caveolae-mediated endocytosis  
 83–4  
 CBP1 (cap-binding protein) 233,  
 234  
 CCR5 80, 82, 400, 407–8, 409  
 CD4 23, 80, **82**  
 downregulation by HIV-1  
 405–6, 407  
 mechanism of HIV-1 entry  
 400, 402  
 CD4<sup>+</sup> T cells 101, 107  
 antigen presentation to 106  
 counts, HIV infection 408, 409  
 HIV infection 106, 408–9  
 regulatory 108–9  
*see also* helper T cells  
 CD8<sup>+</sup> T cells 102, 107  
 antigen presentation to 106  
 HIV infection 408–9  
*see also* cytotoxic T lymphocytes  
 CD21 23, **82**  
 CD155 (Pvr) 253, 254  
 transgenic mouse 464, 465  
 cDNA *see* complementary DNA  
 cell(s)  
 analyzing types infected  
 470  
 antiviral defenses 126–31  
 antiviral state 128, 129  
 fate of virus in 160–1  
 fate of virus-infected 162–4  
 fusion 83, 163  
 growth regulation and subversion  
 392–5, 394  
 immortalization 159–60  
 microanalysis techniques  
 210–11  
 necrosis 162, 162  
 nonpermissive 160  
 primary *see* primary cells  
 removal of nucleus 248  
 semipermissive 161  
 size and organization 16  
 transformation *see* transformation  
 viral nucleic acids 205–9  
 viral proteins 193–204  
 virus entry 21, 80–9  
 virus release 80, 93, 93–4, 95,  
 96  
 virus replication 15–19  
 cell culture 156–60  
 animal and human cells 157,  
 157–60  
 bacteria 156  
 plant cells 156  
 plaque assays 164–5, 165  
 cell death 80  
 pathways 162, 162  
 programmed *see* apoptosis  
 virus-induced 162–3, 164  
 cell lines, continuous 158,  
 159–60, 160  
 cell lysis 80, 163  
 complement-mediated 108,  
 109  
 phage  $\lambda$  373  
 cell-mediated immunity 100, 102  
 measurement 112  
 Centers for Disease Control and  
 Prevention 488, 489  
 central nervous system (CNS)  
 rabies virus spread to 37, 38  
 spread of viruses within 23  
 virus infections 54–6  
 centrifugation  
 equilibrium density gradient  
 174, 175  
 rate zonal (differential) *see* rate  
 zonal centrifugation  
 cervical carcinoma 314–16, 318  
 cesium chloride (CsCl) density  
 gradients 205, 206  
 chemokine receptors 23, 82–3  
 chicken pox 24, 332  
 vaccine **122**  
*see also* varicella zoster virus  
*Chlorella* viruses 9, 376, 376  
 chorioallantoic membrane 165  
 chromatin 214, 216–17  
 structure 223, 224  
 chromium, radioactive 112  
 chromosomes  
 bacterial 214  
 bacterial artificial *see* bacterial  
 artificial chromosomes  
 eukaryotic 214  
 proteins, viral DNA association  
 312  
 small (mini) *see* episomes  
 chronic disease/complications  
 45–7  
 “accidental” damage 50  
 acute infections 49–50, 51  
 hepatitis B virus 25, 415–16  
 persistent infections 50–3, 51  
 Circoviridae **70**  
 circular permutation, T4 genome  
 369  
 cis-acting genetic elements 214  
 cis-acting replication element  
 (CRE) 254  
 CJD *see* Creutzfeldt–Jacob disease  
 classification, virus 66–9, 72–7,  
**76**  
 Baltimore scheme 75  
 disease-based schemes 75–7  
 by virus–host dynamics 44–9  
 clathrin-mediated endocytosis  
 83–4, 84  
 clonal selection 107, 107  
 clones 156  
 cloning 181, 443–54  
 cloning vectors 443–54  
 bacterial artificial chromosomes  
 458–60  
 bacterial plasmids 444–9,  
 448–9  
 cosmids 450, 451  
 DNA animal viruses 451–3,  
**452**  
 gene therapy **491**, 491–3  
 phage  $\lambda$  449–51, 450  
 viral 449–54  
 Closteroviridae **70**  
 Clustal W 478  
 CNS *see* central nervous system  
 co-carcinogens, herpesviruses as  
 354–5  
 co-repressors 221  
 cold, common 23, 30, 49, 266  
 cold viruses 25, 49, 256, 266

- Colorado tick fever virus 295  
*Coltivirus* 295  
 Comoviridae **70**  
 complement fixation (CF) assay  
 115–17  
 complement-mediated cell lysis  
 108, 109  
 complementary DNA (cDNA)  
 164  
 generation by retroviruses 387,  
 388, 389–91, 390  
 integration into host genome  
 389  
 migration into nucleus 388,  
 388–9  
 viral RNA detection by PCR  
 190  
 complementation, analysis of  
 mutations 438, 438–9  
 complementing cell lines 451,  
 453  
 complications *see* chronic  
 disease/complications  
 conditional lethal mutations 161  
 confocal microscopy 199–201,  
 200–1  
 consent, informed 34  
 contact inhibition 158  
 loss of 159–60  
 continuous cell lines 158,  
 159–60, 160  
 copia 396, 397  
 copy number 443–4  
 core particles 363  
 coreceptors 82–3  
 Coronaviridae **70**, 263  
 coronaviruses **29**, **46**, 263–7, **268**  
 cytopathology and disease  
 266–7  
 replication 264–6, 265  
 structure 263, 264  
 Corticoviridae **70**  
*cos* sites 372, 449, 450, 451  
 cosmids 450, 451  
 cowpea mosaic virus 268, **268**  
 cowpox virus 121, 361  
 coxsackieviruses 256, 271  
 CPE *see* cytopathic effects  
 CR2/CD21 23, **82**  
 Creutzfeldt–Jacob disease (CJD)  
 13, 298, 299–300  
 cro protein 372, 373, 375  
 CrPV-like viruses **70**  
 cryoelectron microscopy 148–9,  
 150  
 CTL *see* cytotoxic T lymphocytes  
 cucumber mosaic virus,  
 recombinant vaccine 124  
 culture media 156, 157  
 CXCR4 80, 82, 400, 407–8, 409  
 cyclic AMP (cAMP) 221, 375–6  
 cyclic AMP receptor protein (CRP)  
 221  
 cyclin-dependent kinase-9 (CDK-9)  
 405, 405  
 cyclin-T1 405, 405  
 Cystoviridae **70**  
 cytidine deaminases 131  
 cytochalasin B 248  
 cytotoxic infections 80  
 cytokines 99, 127, 470  
 cytolysis *see* cell lysis  
 cytomegalovirus (CMV) *see* human  
 cytomegalovirus  
 cytopathic effects (CPE) 80, 163  
 plaque assays 164–5, 165  
 quantal assays 169  
 cytopathology 80, 163, 163–4  
 cytoplasmic polyhedrosis virus  
 292  
 cytotoxic T lymphocytes (CTL)  
 107, 162  
 in HIV infection 408–9  
 Dane particles 413  
 databases, biological 474–6, 475  
 applications 476–8  
 composite 475  
 primary 474  
 secondary 475  
 defective interfering (DI) particles  
 161, 454  
 defective virus particles 13, 161  
 cloning/expression vectors 454  
 defensins 99, 135  
 degrees of separation 479  
 delta antigen 296, 297  
*Deltavirus* **70**  
 denaturing gel electrophoresis *see*  
 gel electrophoresis  
 dendritic cells 106  
 dengue fever **29**  
 dengue virus NS3 protease 478  
 deoxyribonucleic acid *see* DNA  
 deoxyribonucleoprotein complex  
 214  
 dependoviruses 324–5  
 desiccation resistance 27  
*Desmodium* yellow mottle virus  
 72, 73, 74  
 dicer 231, 231  
 dideoxycytidine (ddC) 134  
 dideoxyinosine (ddI) 134  
 differential centrifugation *see* rate  
 zonal centrifugation  
 differential display analysis 164  
 dilution endpoint methods  
 169–70, 170  
 disease, viral 19  
 animal models 34–40  
 classification by virus–host  
 dynamics 44–9  
 impact in human history 8–9  
 outcomes 24–5  
 patterns in humans 41–58  
 prevention 33, 120–6  
 prospects for elimination 490  
 symptoms 23–4  
 transmission 24  
 disease-based classification systems  
 75–7  
 distemper 281  
 DNA 69  
 complementary *see*  
 complementary DNA  
 detecting synthesis of viral 205,  
 206  
 double-stranded *see* double-  
 stranded DNA  
 eukaryotic 214–15  
 integration into host *see*  
 integration, viral DNA  
 methylation 223  
 non-protein-encoding 214–15  
 prokaryotic 214  
 quantitative PCR analysis  
 189–90, 190  
 sequence analysis 181–4, 182  
 single-stranded *see* single-  
 stranded DNA  
 terminal redundancy 367,  
 369  
 DNA DataBank of Japan (DDBJ)  
 474  
 DNA end problem 217, 304–5  
 DNA ligase 216, 445  
 DNA methylases 135–6  
 DNA polymerases  
 DNA replication 215, 216  
 eukaryotic 216  
 heat-stable, for PCR 187, 188  
 phylogenetic relationships 11,  
 12  
 viral 217, 218  
 DNA replication 215, 215–17  
 DNA end problem 217, 304–5  
 error rate 247–8  
 eukaryotes 216–17  
 initiation 215, 215–16  
 rolling circle 344, 345, 369,  
 369  
 vegetative 343–4, 345  
 virus-infected cells 217  
 viruses 217, 218  
 DNA vaccines 125  
 DNA viruses 69, 304–5  
 as cloning vectors 451–3

- detection of genome synthesis 205, 206
- DNA replication 217
- genome sequencing 180–1
- plant 325–6
- replication 304–5
- algal viruses 376
- hepadnaviruses 413–18
- “large” bacteriophages 365–76
- large cytoplasm-replicating viruses 360–5
- large nuclear-replicating viruses 331–57
- small and medium-sized viruses 303–28
- ssDNA 305
- structure and size 67
- transcription 232
- tumor-inducing 164
- double-stranded DNA (dsDNA)
- hepadnavirus genome 413–14, 414
- PCR analysis 187–8, 188
- size measurement 185, 185, 186, 187
- double-stranded RNA (dsRNA) 292
- cell defenses 130
- genomes, RNA viruses with 246, 292–5
- induction of interferon 127–8, 129, 295
- drug-resistance markers 445
- drugs, antiviral *see* antiviral drugs
- dsDNA *see* double-stranded DNA
- dsRNA *see* double-stranded RNA
- E1A/E1B proteins 319–20, 320
- E2A/E2B proteins 320
- E4 protein 320, 321
- EBERs *see* Epstein–Barr-encoded RNAs
- Ebola virus 29, 35, 282
- EBV *see* Epstein–Barr virus
- echoviruses 256
- eclipse period 210
- ectromelia virus 464
- ED<sub>50</sub> 130, 169
- Edinburgh Mouse Atlas 474
- effective dose, median (ED<sub>50</sub>) 130, 169
- electron microscope (EM)
- 147–51, 148
- counting of virions 149–51
- DNA genome length measurement 185, 185
- specimen preparation 148, 149
- ELISAs 113, 113–14, 201
- ELISPOT assays 470
- emerging disease 485–90
- bioterrorism and 489–90
- sources and causes 488–9
- encephalitis 54
- mosquito-borne 263
- viruses causing 55–6, 291
- endocytosis
- caveolae-mediated 83–4
- clathrin-mediated 83–4, 84
- lipid-raft-mediated 84
- receptor-mediated *see* receptor-mediated endocytosis
- endonuclease 229–30
- endoplasmic reticulum, rough 93, 94
- enhancers 222–3, 223
- SV40 virus 309
- enteroviruses 55, 271
- Entrez Gene 475
- entry, virus 21, 79, 80–9
- bacteriophages 87–9
- enveloped viruses 84–5, 86–7
- nonenveloped viruses 83–4, 84
- nonspecific methods 89
- plant cells 85–7
- env* gene 385–6, 387, 401
- Env protein 383, 385–6, 389
- envelope, viral 72
- generation 93, 93–4
- enveloped viruses
- entry into cells 84–5, 86–7
- exit from cells 93–4, 95, 96
- fractionation 174
- enzymatic markers, recombinant plasmids 445
- enzyme-linked immunosorbent assays (ELISAs) 113, 113–14, 201
- epidemiology, viral 5–6, 30–3, 31
- role of PCR 190
- epidermal growth factor (EGF) receptor 23, 82
- epinephrine 348, 350
- episomes (mini-chromosomes)
- Epstein–Barr virus 354
- hepatitis B virus 415
- herpes simplex virus 348
- SV40 312, 318
- epitopes 102–4, 103
- buried 103, 104
- conformational 103, 104
- sequential 103, 103
- epizootology 5
- Epstein–Barr-encoded RNAs (EBERs) 352, 353, 354
- Epstein–Barr nuclear antigens (EBNAs) 352, 353
- Epstein–Barr virus (EBV) 29, 45, 332–3
- evasion of immunity 111, 353–4
- genome 353
- as infectious co-carcinogen 354
- latency 52, 351–4, 353
- lymphocyte immortalization 159, 352–3
- pathology of infection 354
- reactivation 353–4
- tissue tropism 23
- equilibrium density gradient centrifugation 174, 175
- equine encephalitis viruses 46, 56
- equine infectious anemia virus (EIAV) 399
- error frequency, RNA replication 247–8
- Escherichia coli*
- culture 156
- fertility (F<sup>+</sup>) factor 458–60
- HflA protease 375–6
- injection of phage DNA 87–9, 88
- lac* operon 219, 219, 220–1
- phage receptors 87, 88
- phagemid vectors 451
- plaque assay 165
- plasmids as cloning vectors 444–9, 446
- recA protease 375
- replication of DNA phages 365–76
- RNA polymerase 219, 220, 370, 370
- size and organization 16
- ethidium bromide 187
- etiology, viral 44
- eubacteria 9–10, 10
- euchromatin 223, 224
- eukaryotes 9–10, 10
- DNA replication 216–17
- virus-infected cells 217
- genome organization 214–15
- transcription 221–32
- translation 233–4, 234
- transposable elements 396
- eukaryotic initiation factors (eIFs) 233, 234
- European Bioinformatics Institute 478
- European Molecular Biology Laboratory (EMBL) 474
- evolution
- impact of virus–host interaction 9
- origin of viruses 9–11
- persistent viral infections 42–4
- transposable elements 397

- exocytic vesicles 94  
 exocytosis, virus 94, 96  
 exons 225  
 exonucleases 216, 229  
 explantation 39  
 exportins 285  
 expression vectors, viral 452, 452–3  
  
 F pilus 87, 89  
 Fab region 196, 197  
 Fc region 113, 196, 197  
 fecal–oral transmission 28, 256  
 feeder layer 39  
 feline immunodeficiency virus (FIV) 399  
 feline panleukopenia 324  
 fertility (F') factor 458–60  
 fetal infections 110–11  
 fibronectin 82  
 Filoviridae 70, 275  
 filoviruses 282  
 Finkel-Biskis-Jenkins murine sarcoma virus 393  
 Flaviviridae 70  
 flaviviruses 46  
   replication 256–7, 257  
 flu *see* influenza  
 fluorescent in situ hybridization (FISH) 208, 470  
 fluorescent-labeled antibodies 199–201, 200–1  
 fluorography 208, 209  
 fluors 189  
 foamy viruses 382  
 focus of infection 165  
 focus of transformation 166, 166, 314  
 foot pad inoculation 39, 466, 466–7, 467  
 forensics 190  
 formaldehyde (formalin) 123  
*Foveavirus* 70  
 fractionation  
   techniques 174–6, 175  
   viral nucleic acids 185–6  
   viral structural proteins 176–9, 177  
*Furovirus* 70  
 Fuselloviridae 70  
 fusion, membrane 85, 86–7  
 Fuzeon 134  
  
*gag* gene 385–6, 387, 401  
 Gag-Pol fusion protein 383–4, 385  
   retrotransposons 396, 397  
 Gag protein 383  
   retrotransposons 396, 397  
   synthesis 391, 392, 392  
 gancyclovir 132, 133, 357  
 gastroenteritis 295  
 gel electrophoresis 176  
   capsid proteins 178, 178–9, 179, 180  
   DNA sequencing 183  
   pulse labeling studies 194, 195  
   viral genome size measurement 186, 187  
   viral proteins 176–7, 177  
 Geminiviridae 70  
*Geminivirus* 85, 325–6  
 GenBank 474, 475  
 gene(s)  
   bacterial 214  
   cellular, induced by viruses 164  
   databases 475  
   directed mutagenesis of viral 454–6, 457  
   expression, viral 79  
   inducible 220  
   large nuclear-replicating DNA viruses 331–2  
   mutations *see* mutations  
   overlapping,  $\Phi$ X174 bacteriophage 326, 327  
   phylogenetic relationships of viral 10–11, 12  
   transposition 395–6  
 gene therapy 452, 453, 491, 491–3  
 genetic markers, selectable 445  
 genetic recombination 124  
 genetics  
   molecular 435–62  
   reverse 443  
   virulence 467  
 genomes, viral 3–4, 65, 69  
   ambisense 290, 291, 292  
   characterization 179–90  
   cloning vectors 443–54  
   compression 326, 327  
   cryoelectron microscopy 149, 150  
   databases 474, 475  
   detection of synthesis 205  
   enzymatic modification by cells 131  
   fate in abortive infections 160–1  
   insertion into cells 89, 90  
   integration into host DNA *see* integration, viral DNA  
   isolation 179, 181  
   large nuclear-replicating DNA viruses 331–2  
   maintenance in cells 161  
   map units (mu) 441–2  
   monopartite 274  
   multipartite *see* segmented genomes  
   PCR analysis 187–90  
   replication 79  
   representation methods 441–2  
   restriction mapping 442–3, 443–4  
   segmented *see* segmented genomes  
   separation from cellular 205, 206  
   sequence analysis 180–4, 474  
   size measurement 184–6  
   size range 4  
   genotype 5  
 German measles *see* rubella  
 glycoproteins  
   cell surface 80, 81  
   viral 84–5, 86–7  
   formation 93, 93–4  
   role in budding 94, 95  
   stoichiometry 178  
 Golgi apparatus 93, 94, 106  
 granulin 355  
 granulosis viruses (GVs) 355–6  
 green fluorescent protein (GFP) 468, 470  
 growth factors 50  
 Guanarito virus 292  
 guinea pig models, latent HSV infection 40  
 gut-associated lymphoid tissue 22  
 gypsy 396, 397  
  
 HAART 134–5  
 hairpin loops 305, 323–4, 324  
 Hantaan virus 291  
 hantavirus adult respiratory distress syndrome (HARDS) 291  
 hantaviruses 27, 47, 289, 489  
   pathogenesis 291  
   replication 289–90  
   respiratory disease 48  
 Harvey murine sarcoma virus 393  
 HeLa cells 157–8  
 helical viruses 69  
   capsid assembly 89–91, 91  
 helicases 215, 216  
 helper T cells 101  
   Th1/Th2 response 99, 101–2  
   *see also* CD4<sup>+</sup> T cells  
 helper viruses 13, 324–5  
 hemagglutination (HA) assay 152–3, 153, 169  
 hemagglutination inhibition (HI) test 114–15, 116, 169  
 hemagglutination (HA) units 152

- hemagglutinin  
 drugs targeting 132–3  
 flu strains 287–8
- hemorrhagic fevers, viral 282,  
 291, 292, 489
- Hepadnaviridae **70**
- hepadnaviruses 47, 413–18  
 evolutionary origin 417  
 replication cycle 415  
 virion and genome 413–15,  
 414
- hepatitis 23, 56–8, 418
- hepatitis A virus **29, 46, 57**  
 replication 249  
 vaccine **122**
- hepatitis B core antigen (HBc)  
 413
- hepatitis B virus (HBV) **29, 47,**  
 57  
 case study 418  
 chronic disease 25, 416–17  
 hepatitis delta virus and 57–8,  
 296, 297  
 pathogenesis 415–16  
 vaccine **122, 124–5**  
 virion and genome 413–15,  
 414
- hepatitis C virus (HCV) **29, 46,**  
 57, 487–8
- hepatitis delta virus (HDV) 13,  
**29, 296–7**  
 disease 47, 57–8  
 replication 296, 296–7  
 RNA editing 232, 297
- hepatitis E virus **29, 46, 58**
- hepatocellular carcinoma (HCC)  
 416
- hepevirus **46**
- herd immunity 30
- herpes simplex virus (HSV) **29**  
 $\alpha$ -TIF protein (VP16) 340,  
 341–3, 342  
 animal models 37–40, 39  
 antiserum 196  
 atomic force microscopy 152  
 capsid formation 344, 346–7  
 capsid proteins 179, **179, 334**  
 cryoelectron microscopy 149,  
 150  
 cytopathological effects 163,  
 163  
 DNA replication 217, 218,  
 343–4, 345, 346  
 drug treatment 132, 135  
 encephalitis 55–6  
 entry into cells 83, 85, 340–1,  
 340–1  
 evasion of immunity 110–12,  
 164, 351
- gene therapy vector 491–2,  
 492
- genome 334–8, 335, **336–7**
- genomic DNA  
 cloning 447–9, 448–9  
 PCR analysis 188, 189  
 separation from cellular DNA  
 205, 206  
 sequencing 182, 183  
 size measurement 185, 185
- glycoproteins 340, 340
- immune response 106
- immunoaffinity chromatography  
 204, 204
- latency-associated transcripts  
 (LATs) *see* latency-  
 associated transcripts
- latent infections 17, 25, 52,  
 333, 347–51, 349  
 animal models 37–40, 39  
 in situ hybridization analysis  
 208, 208  
 reactivation 52, 348–51,  
 350  
 transcription during 342,  
 348–9, 350
- mRNA  
 hybridization 206–7, 207  
 in vitro translation 209, 210  
 microarray analysis 211  
 splicing 228–30, 230–1
- pathology of infection 354
- plaque assays 165, 167, 167–8
- productive infection (vegetative)  
 cycle 338–44, 342  
 cascade of gene expression  
 338–9, 339  
 early gene expression 343  
 genome replication/late gene  
 expression 343–4, 345  
 immediate-early gene  
 expression 341–3  
 virus assembly and release  
 344
- pulse labeling studies 194–5,  
 195
- quantal assay 169–70, 170
- recombinants 439, 439–40,  
 441, 456–8, 459–61
- replication 334–51
- spread within host 23
- symptomatic disease 23–4
- target tissues 55
- thymidine kinase (TK) 132,  
 440–1
- transmission 28
- type 1 (HSV-1) 37, **45, 332**  
 analysis of spread within host  
 468, 468, 469
- genome 334–8, 335, **336–7,**  
 441–2
- glycoprotein C (gC)-negative  
 mutants 83
- latency 348
- virulence assays **466, 466–7,**  
**467**
- type 2 (HSV-2) 37, **45, 332**  
 guinea pig model 40  
 latency 348  
 virion 334, 334
- herpes zoster virus *see* varicella  
 zoster virus
- Herpesviridae **70**
- herpesvirus entry mediators  
 (HVEMs) **82, 340, 340–1**
- herpesvirus suis *see* pseudorabies virus
- herpesviruses **45, 332–5**  
 alpha- 332  
 antiviral drugs 132  
 beta- and gamma- 332–3  
 control measures 33  
 DNA replication 217, 218  
 evolutionary origin 11  
 exit from cells 94, 96  
 gene therapy vectors **452, 491**  
 genetic complexity 333  
 immunosuppressed individuals  
 112  
 latency 25, 52, 333, 347–54  
 pathology of infections 354–5  
 phylogenetic relationships 376,  
 376  
 replication 304, 333–44  
 transmission 24
- heterochromatin 223, 224
- HEV-like virus **70**
- hexons 72, 74
- high throughput (HT) technologies  
 473, 474, 479–81
- highly active antiretroviral therapy  
 (HAART) 134–5
- histones 216–17, 223, 224  
 viral DNA association 312
- HIV **29, 47, 383**  
 CCR5 or CXCR4 tropism  
 407–8, 409  
 cellular defenses 131, 401–4,  
 404  
 cloning/expression vectors 453  
 coreceptors 82–3, 400, 402,  
 406–8  
 drug-resistance database 475  
 entry into cells 400, 402  
 evasion of immunity 111–12  
 gene therapy vectors **491**  
 genetic map 387, 401  
 immune system destruction  
 406–10

- HIV (*cont'd*)  
 incubation period 53  
 infection  
   case study 410  
   control measures 33, 410  
   drug therapy 134–5, 409, 409–10  
   emergence 485–6, 486, 487, 488  
   epidemic 33, 399–400  
   JC virus infections 308, 327–8  
   Kaposi's sarcoma 355  
   opportunistic infections and neoplasms 54  
   pathogenesis 408, 408–10  
   symptomatic disease 23  
   *see also* AIDS  
 integration into host genome 404–5  
 origins 48, 399–400  
 receptors 80, 400, 402  
 recombinant virus-mediated destruction 493  
 related lentiviruses 399  
 replication 400–6, 403  
 routes of entry 22, 406  
 surface glycoprotein (SU or gp120) 400, 402, 405  
 T cell infection 106  
 tissue tropism 23  
 transmembrane glycoprotein (TM or gp41) 400  
 transmission 6–7, 24, 28  
   type 1 (HIV-1) 399–410  
   type 2 (HIV-2) 399–400  
*Hordeivirus* 70  
 host  
   analysis of virus spread 467–9, 468, 469  
   effect of virus infections 4–6  
   fate of infected 24–5  
   interactions with viruses *see* virus–host interactions  
   range 43, 80  
   response, characterization methods 470–1  
   transmission of virus from 24  
   virus entry 20–1, 21  
   virus spread within 21–3  
 host defenses 19, 20, 98–117  
   *see also* immune response; immunity  
 HPV *see* human papillomaviruses  
 HSV *see* herpes simplex virus  
 HTLV *see* human T-cell leukemia virus  
 human  
   experimental studies 34  
   history, impact of viral disease 8–9  
   patterns of viral disease 41–58  
   reservoirs of infection 28  
   viruses infecting 45–7  
 human–virus interactions, dynamics 42–9  
 human cytomegalovirus (HCMV) 45, 332  
   case study 357  
   evasion of immunity 111  
   immunosuppressed individuals 52, 354, 357  
   protein localization methods 199–200, 200–1  
 human herpes virus-6 (HHV-6) 45, 332  
 human herpes virus-7 (HHV-7) 45, 332  
 human herpes virus-8 (HHV-8) 45, 332–3, 354–5  
   protein interaction map (PIM) 481, 482  
 human immunodeficiency virus *see* HIV  
 human papillomaviruses (HPV) 314–18  
   disease 45, 50–2  
   replication and cytopathology 316–18, 317  
   type 16 (HPV-16) 318  
   genome 316, 316  
   type 18 (HPV-18) 316, 318  
   vaccines 122, 125, 318  
 human T-cell leukemia virus (HTLV) 29, 47  
   complications 52  
   genetic map 386, 387  
   transformation 395  
 humoral immunity 100, 102  
 HVEMs *see* herpesvirus entry mediators  
 hybridization, nucleic acid 205–7, 207  
 hybridoma cells 196–7, 198  
 5-hydroxymethyl cytosine (5'-OHMeC) 369  
 Hypoviridae 70  
 hypoxanthine-guanine phosphoribosyltransferase (HGPRT) 196–7, 198  
 ICAM *see* intercellular adhesion molecule  
 icosahedral viruses 69  
   capsid assembly 92, 92–3  
   structure 72, 73, 74  
 ID<sub>50</sub> 169  
*Ideaovirus* 70  
 IFN *see* interferon  
 immune memory 108, 108  
 immune response 22, 24, 97–117, 98  
   measurement 112–17  
   viral pathogenesis studies 470–1  
 immune system 98  
 immune tolerance 110–11  
 immunity 5  
   active evasion 111–12  
   adaptive 20, 98, 100–8  
   cell-mediated 100, 102, 112  
   control and dysfunction 108–9  
   herd 30  
   humoral 100, 102  
   innate 98–9  
   passive evasion 110–11  
   specific viral responses 109–12  
   vaccine-stimulated 123, 124  
 immunoaffinity chromatography 202–3, 203–4, 204  
 immunofluorescence methods 198–201, 199  
 immunohistochemistry 470  
 immunological assays 470  
 immunologically naive individuals 5  
 immunosuppression  
   herpesvirus reactivation 354  
   virus-induced 111  
   virus infections complicating 112  
 in silico analysis 473–4  
 in situ hybridization 207–9, 208, 209, 470  
 in vitro translation 209, 210  
 inapparent infections 19  
 incubation periods 20, 21–3  
   diseases with long 53–4  
   mortality rate and 44, 53  
 index case 31  
 infections, virus 4–6  
   abortive 160–1  
   cellular outcome 160–4  
   eclipse period 210  
   inapparent or asymptomatic 19  
   latent *see* latent infections  
   lysogenic *see* lysogeny  
   mixed *see* mixed infections  
   nonproductive 160–1  
   pathogenesis *see* pathogenesis, viral  
   persistent *see* persistent infections  
   prevention 33, 120–6  
   productive 15, 17, 160  
   statistical analysis 168  
   targeting specific organ systems 54–8  
   treatment 120

- infectious disease  
 emerging 485–90  
 mortality trends 486  
 prospects for elimination 490  
*see also* disease, viral
- infectious dose, median (ID<sub>50</sub>)  
 169
- infectious mononucleosis 111,  
 352
- infectious units of virus 169–70
- influenza (flu) 49  
 avian 8, 33, 48, 288  
 control 33  
 drug treatment 132–4  
 epidemics/pandemics 8, 48, 49,  
 285–8, 287  
 Spanish pandemic *see* Spanish  
 influenza epidemic  
 (1918–19)  
 vaccine 122
- influenza virus 29, 46, 283–8  
 antigenic variation 285–8, 287  
 avian strains 287  
 entry into cells 82  
 enumeration 152–3, 153  
 H1N1 (1918) strain 48, 49,  
 486–7  
 H5N1 strain 8, 33, 48, 83,  
 288, 487  
 interferon-induced defenses  
 128  
 M1 protein 285  
 mixed infections 285, 287,  
 488  
 NP protein 285  
 NS2 protein 285  
 PB1 and PB2 polymerase  
 subunits 285  
 PCR analysis 190  
 replication 284–5, 286  
 strains 287–8  
 structure 284, 284  
 swine strains 287  
 type A 48, 132–4, 283–8  
 type B 283  
 type C 283
- initiation codon, translation 233,  
 235  
 Q $\beta$  bacteriophage 270, 271  
*see also* AUG initiation codon
- initiation factors (IFs)  
 eukaryotic (eIFs) 233, 234  
 prokaryotic 235, 235
- initiator transfer RNA (tRNA)  
 233, 235
- innate immunity 98–9
- inoculation 27, 28  
 animal models 35, 36, 466–7  
 route of 466, 466, 467
- Inoviridae 70, 451
- insect viruses 355–6
- Institutional Animal Care and Use  
 Committee (IACUC)  
 465–6
- int* gene 385–6
- integrase 383  
 cDNA transport into nucleus  
 388–9  
 HIV-1 400  
 integration of cDNA into  
 genome 389
- integration, viral DNA 217  
 adeno-associated virus 325  
 Epstein–Barr virus 354  
 gene therapy vectors 453  
 HIV-1 404–5  
 phage  $\lambda$  375  
 retroviruses *see under*  
 retroviruses  
 SV40 virus 314, 315
- intercellular adhesion molecule  
 (ICAM) 80, 82, 82
- interference 161
- interferon (IFN) 19, 24, 126–30,  
 164  
 antiviral activity 128, 129,  
 130  
 induction 127–8, 129, 295  
 measurement of activity  
 128–30  
 types I and II 127
- interferon (IFN)- $\alpha$  127, 223–4,  
 224–5
- interferon (IFN)- $\beta$  127
- interferon (IFN)- $\gamma$  127
- internal ribosome entry site (IRES)  
 249–51, 250–1
- International Committee on  
 Taxonomy of Viruses  
 (ICTV) 66–7, 70–1, 77
- internet resources 504–5  
 bioinformatics 481, 483
- intracerebral (i.c.) inoculation 35
- intracranial (i.c.) inoculation 466,  
 466–7, 467
- intravenous (i.v.) inoculation 466
- introns 225
- iodouridinedeoxyriboside (IUdR)  
 135
- iontophoresis 40
- IRES *see* internal ribosome entry  
 site
- Iridoviridae 70, 376
- isoforms 298
- Jak-STAT signal transduction  
 cascade 224, 224–5
- Japanese encephalitis, vaccine 122
- JC virus 45, 52, 308  
 case study 327–8
- Jenner, Edward 121, 122
- journals, virology 503
- Junin virus 292
- Kaposi's sarcoma (KS) 354–5
- Kaposi's sarcoma herpesvirus *see*  
 human herpes virus-8
- keratitis, HSV 354
- Kirsten murine sarcoma virus 393
- knock-out (KO) mice 471
- Koch's rules 34
- Kozak sequence 233, 234
- kuru 13, 298
- La Crosse encephalitis virus 29,  
 47  
 replication 289, 290  
 laboratory protocols 503–4
- lac* operon 219, 219, 220–1
- lacZ* *see*  $\beta$ -galactosidase
- lagging strand 215, 216
- $\lambda$  arms 449–50
- $\lambda$  bacteriophage 88–9  
 biochemistry of lytic/lysogenic  
 decision 374, 375–6  
 CI repressor 373, 373–5  
 CII and CIII proteins 373–5  
 cloning using 449–51, 450  
 cro protein 372, 373, 375  
 DNA size measurement 186,  
 187  
 early events after infection  
 372–5, 374  
 genome 372, 373  
 lysogeny 372, 373–5  
 N protein 372, 373, 374–5  
 plaque assay 165  
 productive/lytic infection 372,  
 373  
 replication 370–6
- $\lambda$  lysogen 375
- large T antigen 309, 310, 311,  
 312  
 abortive infections 313–14,  
 315  
 synthesis 306–7, 309, 312
- laser capture microdissection  
 (LCM) 470
- Lassa fever virus 292
- Last Universal Common Ancestor  
 (LUCA) 11
- latency-associated transcripts  
 (LATs) 342, 348–51  
 detecting and locating splices  
 228–30, 230–1  
 function 350–1  
 in situ hybridization 208, 208

- latent infections 161  
   animal models 37–40, 39  
   evasion of immunity 110  
   herpesviruses *see under*  
     herpesviruses  
   in situ hybridization analysis  
     208, 208  
   PCR analysis 189–90  
   phage  $\lambda$  372  
 LD<sub>50</sub> 169, **466**, 466–7, **467**  
 LDL receptor **82**  
 leading strand 215, 216  
 lentiviruses 47, 382, 383,  
   399–410  
   cloning/expression vectors **452**,  
     453  
   gene therapy vectors **491**  
   replication 386, 400–6  
   structure 384  
   *see also* HIV  
 lethal dose, median (LD<sub>50</sub>) 169,  
   466, **466**, **467**  
 leucine zipper proteins 296  
 Leviviridae **70**, 269  
 light microscope 148  
 linker-scanning mutagenesis 456  
 lipid-raft-mediated endocytosis 84  
 liposomes 89  
 Lipothrixviridae **70**  
 liver  
   cancer 57, 416  
   viral infections 56–8  
 long interspersed elements (LINEs)  
   396  
 long terminal repeats (LTRs) 386  
   generation 387, 388, 389–91,  
     390  
   HIV-1 404–5  
   integrated retroviruses 389  
   retrotransposons 396, **396**  
   retroviral cDNA expression  
     391  
 luciferase 468–9, 469  
 Luteoviridae **70**  
 lymph nodes 100, 101  
   immune functions 106, 107,  
     108  
 lymphatic system 100, 100–1  
   route of entry of viruses 22  
   viruses replicating in **22**  
 lymphocytes 24, 100–1  
   clonal selection 107, 107  
   culture 158–9  
   EBV latent infection 351–4  
   stimulation index 112  
   *see also* B lymphocytes; T  
     lymphocytes  
 lymphocytic choriomeningitis virus  
   (LCMV) 111, 292  
 lymphoid tissue, gut-associated 22  
 lysis, cell *see* cell lysis  
 lysogeny 4, 17, 372  
   biochemical decision 374,  
     375–6  
   establishment 373–5  
   priming cell for 373  
 M13 bacteriophage  
   site-directed mutagenesis system  
     456, 457  
   ssDNA cloning 451  
 M13mp/pUC vectors 451  
 Machupo virus 292  
 macrophages  
   antigen processing 104–5  
   HIV infection 22, 82, 407–8  
   lentivirus infection 389, 399  
 macropinocytosis 84  
 mad cow disease 13, 298,  
   299–300  
 maedi/visna virus (MVV) 399  
 magnetic resonance imaging (MRI),  
   whole-body 468, 469  
 maize streak virus 326  
 major histocompatibility complex  
   (MHC) 104  
   type I (MHC-I) **82**  
     antigen presentation 104,  
       104–6, 162  
     inhibition of antigen  
       presentation 111–12,  
       164  
     interferon actions **130**  
   type II (MHC-II) **82**, 105,  
     106  
 male specific phages 89  
 map units (mu), genome 441–2  
*Marafivirus* **70**  
 Marburg virus 282  
 maturational proteases 92  
 MAVS protein 127–8  
 MC29 avian myelocytoma virus  
   **393**  
 McClintock, Barbara 395  
 measles 281  
   complications 53  
   eradication 33, 490  
   problems with vaccination 126  
   vaccine **122**  
 measles virus **29**, 47, 280  
   persistence within host 25, 53  
 melting 356  
 membrane proteins, integral 80,  
   81  
 memory, immune 108, 108  
 meningitis 54  
   viral (aseptic) 55, 271  
 mental illness 283  
 messenger RNA (mRNA)  
   capping *see* capping, mRNA  
   degradation 130  
   editing 231, 232  
   expression 217–32  
     *see also* transcription  
   hybridization 205–7, 207  
   in situ hybridization 207–9,  
     208  
   in vitro translation 209, 210  
   microarray analysis 211, 211  
   polyadenylation *see*  
     polyadenylation, mRNA  
   polycistronic 235  
   posttranscriptional processing *see*  
     posttranscriptional  
       processing  
   splicing *see* splicing, mRNA  
   subgenomic *see* subgenomic  
     mRNA  
   translation *see* translation  
   turnover 195  
 metastasis 318  
 Metaviridae **70**  
 methylation, DNA 223  
 MHC *see* major histocompatibility  
   complex  
 microarray analysis 164, 210–11,  
   211  
 microchip technology 114, 164,  
   210–11  
 microglial cells 399  
 microRNAs (miRNAs) 130, 214,  
   231  
 microtome 208  
 Microviridae **70**  
 mimivirus 4, 149, 150  
 mink transmissible encephalopathy  
   299  
 minute virus of mice (MVM)  
   324, 325  
 miRNAs *see* microRNAs  
 mitochondrial antiviral  
   signaling (MAVS) protein  
     127–8  
 mixed infections  
   defective virus particles 454  
   influenza virus 285, 287, 488  
 MOI *see* multiplicity of infection  
 molecular biology, resources  
   503–4  
 molecular genetics 435–62  
   goals 435–6, 436  
   tool kit 436, 441–60  
 molecular mimicry 109  
 molecular pathogenesis 463–71  
 Moloney murine sarcoma virus  
   **393**  
 monkey pox 36

- monoclonal antibodies 196–7, 198  
 monocytes **22**  
 Mononegavirales 275–83  
 monopartite genomes 274  
 Montague, Lady Mary Wortly 121  
*Morbillivirus* *see* measles virus  
 mortality rates  
   evolutionary constraints 42  
   incubation periods and 44, 53  
   virus infections with high 48  
 mosaicism 17  
 mosquitoes 24, 256, 263, 291, 488  
 mouse mammary tumor virus (MMTV) 386, 387  
 mouse models  
   latent HSV infection 39, 39  
   poxviruses 35–7  
   rabies 37, 38  
   route of inoculation **466**, 466–7, **467**  
   SCID-hu hybrid 464–5  
   transgenic *see* transgenic mice  
 mouse myeloproliferative leukemia virus **393**  
 mouse polyomavirus (Py) 306, 308  
   in situ hybridization analysis 208, 208–9  
   replication 308  
 mouse pox 35, 36  
 mRNA *see* messenger RNA  
 MS2 bacteriophage **88**, 89  
 multipartite genomes *see* segmented genomes  
 multiple cloning sites (MCS) 445  
 multiple sclerosis (MS) 52–3, 109  
 multiplicity of infection (MOI) 166, 167–8  
 mumps 280–1  
   vaccine **122**  
   virus 47, 280  
 murine leukemia virus (MLV) 95, 386, 387, 393–4  
 murine polyomavirus *see* mouse polyomavirus  
 murine sarcoma virus **393**  
 mutagenesis 454–6  
   linker-scanning 456  
   site-directed 456, 457  
 mutations 437–8  
   analysis 438, 438–40, 439  
   back 123  
   conditional lethal 161  
   frame shift 438  
   isolation 440–1  
   reversible 438  
   RNA viruses 248, 437  
   screening 439, 441  
   selection 439, 440–1  
   temperature-sensitive (*ts*) 161, 439, 439–40  
 Mx protein 128, **130**  
 myelitis 54  
 myeloma cells 196–7  
 Myoviridae **71**  
 myristoylation 251  
 myxoma virus 13, **29**, 36  
  
*Nairovirus* **289**  
 nairoviruses 289–90  
 nanotechnology 493–4  
*Nanovirus* **71**  
 nanowires 494  
 Narnaviridae **71**  
 nasopharyngeal carcinoma 354  
 National Center for Biotechnology Information (NCBI) 475, 475, 476  
 necrosis 162, 162  
*nef* gene 400, 401  
 Nef protein 405–6, 407  
 negative (–)-sense RNA viruses 75, 274–92  
   classification 274  
   with monopartite genomes 274, 275–83  
   with multipartite (segmented) genomes 274, 283–92  
   origin 274–5  
   replication 246, 274–92  
 neonatal infections 110–11, 354  
 neoplasms  
   opportunistic 54  
   virus-induced 52  
   *see also* cancer; tumors  
 nervous system  
   virus infections 54–6  
   virus spread within 23  
 networks 479  
   random 479, 480  
   scale-free (small-world) 479–81, 480  
 neuraminic acid 134  
 neuraminidase, flu strains 287–8  
 neuroinvasiveness 464, **466**, 467  
 neurotropic viruses 23  
 neurovirulence 467  
 neutralization tests 114, 115  
 Newcastle disease 124  
*Nidovirales* 263, 264  
 Nodaviridae **71**  
 nonenveloped viruses  
   entry into cells 83–4  
   fractionation 174–6  
 nonproductive infections 160–1  
 nonstructural proteins 173–4, 193  
 northern blots 202  
 nosocomial infections 31–2  
 nuclear localization signals (NLS) 405, 406  
 nuclear polyhedrosis viruses (NPsVs) 355–6  
 nuclear retention signals (NRS) 405, 406  
 nucleases 176, 185–6  
*Nucleic Acid Research* 476  
 nucleic acids, viral 69  
   characterization in infected cells 205–9  
   detection in infected cells 205  
   fractionation 186  
   hybridization 205–7, 207  
   probes 174, 206  
   separation and digestion 176  
   *see also* DNA; RNA  
 nucleocapsids  
   coronavirus 263, 264  
   influenza virus 285  
   vesicular stomatitis virus 276, 277  
 nucleoprotein 69  
 nucleotide sequences  
   databases 474  
   similarity searching tools 476, 477  
 nucleus  
   herpesvirus replication 340–1, 341, 344, 346  
   influenza virus replication 284, 286  
   lentivirus replication 400–1  
   retroviral cDNA migration into 388, 388–9  
   virus replication not requiring 248  
  
 occluded viruses (OVs) 355–6  
 Oct1 341, 342  
 Okazaki fragments 215  
 2',5'-oligoA synthetase 128, **130**  
 ompC 88  
 oncogenes 52, 313  
   cellular (*c-onc*) 386, 392  
   viral (*v-onc*) 386, 387, 392–3, **393**  
 oncogenesis, papillomavirus-mediated 318  
 oncornaviruses 382, 383  
   expression vectors 453  
   genetic maps 386, 387  
   replication 386–91  
   structure 384  
   transformation mechanisms 392–5

- open translational reading frames (ORFs) 233–4  
 cryptic 234, 258, 261  
 positive-sense RNA viruses 249, 257–8, 259  
 RNA bacteriophages 269–70  
 small and medium-sized DNA viruses 309, 310
- operators 219, 219, 220–1
- operons 219, 219
- Ophiiovirus* 71
- opportunistic infections 54
- ORFeome 479
- ORFs *see* open translational reading frames
- origin-binding proteins 216, 217, 218
- origins of replication (ori) 216  
 bacterial plasmids 445  
 herpesvirus 338, 345  
 SV40 virus 306–7, 309
- Orthomyxoviridae 71
- orthomyxoviruses 46, 283–8  
*vs.* paramyxoviruses 283, 283–4
- Orthoreovirus* 295
- Ourmiavirus* 71
- P22 bacteriophage 92, 92–3
- p53 protein 314, 394  
 adenovirus interaction 320  
 EBV interaction 352–3  
 HPV interaction 318  
 SV40 virus interaction 309, 311, 313–14
- packaging signals 91, 345  
 viral vectors 449, 453, 454
- palindromic sequences 136
- Papillomaviridae 71
- papillomaviruses 29, 305  
 cytopathology 316–18, 317  
 evasion of immunity 110  
 genome 316, 316  
 replication 314–18  
*see also* human papillomaviruses
- papovaviruses  
 replication 305–18  
*vs.* adenoviruses 319
- parainfluenza 275
- parainfluenza virus 280
- Paramecium bursaria Chlorella-1* virus (PBCV-1) 376
- Paramyxoviridae 71, 275
- paramyxoviruses 47, 280–2  
 pathogenesis of disease 280–2  
 replication 280  
*vs.* orthomyxoviruses 283, 283–4
- particle to PFU ratio 166
- Partitiviridae 71
- Parvoviridae 71
- parvoviruses 27  
 replication 305, 323–5  
 therapeutic applications 325
- passage  
 cultured cells 160  
 serial 122–3  
 virus 37
- Pasteur, Louis 121, 122
- pathogenesis, viral 4–5, 19–25, 20  
 animal models 34–40, 464–6  
 characterization of host response 470–1  
 methods for studying 466–70  
 molecular techniques 463–71  
 stages 19–25
- pathogenicity 5
- pBR322 plasmid 445, 446
- PCNA 216
- PCR *see* polymerase chain reaction
- Pecluvirus* 71
- pencyclovir 133
- pentons 72, 74
- peroxidase 201
- persistent infections 4, 17, 25, 161  
 adenoviruses 323  
 complications 52–3  
 dynamics in human populations 42–4, 43  
 hepatitis B virus 415–16  
 patterns in humans 50–3, 51  
 polyomaviruses 308, 314–16, 318  
 stability of association with humans 44–8  
 viruses causing 45–7
- Peyer's patches 22
- PFU *see* plaque-forming units
- pGEM plasmids 445, 446
- phagemids 450, 451
- phages *see* bacteriophages
- $\Phi$ X174 bacteriophage 326, 327, 474
- Phlebovirus* 289
- phleboviruses 290
- Phycodnaviridae 71
- phylogenetic trees 10, 10, 11, 12
- physical contact, spread by 28
- Picornaviridae 71
- picornaviruses 46  
 cytopathology and disease 254–6  
 replication 249–54
- pili 451
- pilot proteins 88, 88, 92–3
- placebos 34
- plant cells 16, 17  
 culture 156  
 defenses against viruses 130  
 virus entry 85–7
- plant models of disease 35
- plant pathogens, subviral 296
- plant viroids 297–8, 298  
*vs.* hepatitis delta virus 296
- plant viruses 8–9  
 assays 165, 165  
 with DNA genomes 325–6, 416–17  
 with RNA genomes 267–9
- plaque, virus 114, 130, 165
- plaque assays 156, 164–5, 165  
 examples 167, 167, 167–8  
 interferon 129–30
- plaque-forming units (PFUs) 165, 166, 167, 168
- plaque reduction assay 128–30
- Plasmaviridae 71
- plasmid-like replication 318
- plasmids, bacterial  
 cloning using 444–54, 448–9  
 cosmid vectors 450, 451  
 genetic maps 444–5, 446
- plasmodesmata 85–7
- platelet-derived growth factor (PDGF) 393, 394
- pneumoviruses 280
- Podoviridae 71
- Poisson analysis 168
- pol* gene 385, 386, 387, 401
- Pol protein *see* reverse transcriptase
- polio(myelitis)  
 eradication 33, 126, 490  
 paralytic 24, 50, 256
- poliovirus 46, 268  
 capsid assembly 92, 254, 255  
 capsid proteins (VP0–VP4)  
 pulse labeling 194, 195  
 stoichiometric analysis 178, 178, 179  
 synthesis 250, 251, 252  
 cytopathology and disease 50, 163, 254–6  
 genetic map 249, 250  
 receptor 23, 80, 82, 252–3, 254  
 replication 249–54  
 cycle 252–4, 253  
 in enucleated cells 248  
 expression of proteins 249–52, 250–1  
 serotypes 255  
 spread within host 22  
 tissue tropism 23  
 transgenic mouse model 464, 465

- transmission 28, **29**, 256  
vaccines **122**, 256  
  problems 123–4, 126  
  Sabin 122, 126  
  Salk 123  
VPg protein 249, 250, 254  
polyA polymerase 225  
polyadenylation, mRNA 225, 227  
  negative-sense RNA viruses  
  276–7, 285  
  positive-sense RNA viruses  
  249, 258, 259, 266, 267,  
  **268**  
  retroviruses 391  
  small and medium-sized DNA  
  viruses 310, 321  
polyadenylation signals 225  
Polydnaviridae **71**  
polydnaviruses 9, 111  
polyhedrin 355, 356, 452  
polymerase chain reaction (PCR)  
  164, 187–90, 188  
  as epidemiological tool 190  
  real time, viral DNA  
  quantitation 189–90, 190  
  reverse transcription (RT-PCR)  
  470, 486  
  RNA detection 190  
Polyomaviridae **71**  
polyomaviruses **45**, 50–2  
  capsid structure 305, 306  
  in situ hybridization analysis  
  208, 208–9  
  replication 305–14  
polythetic groups 77  
Pomovirus **71**  
populations  
  control of disease in 33  
  dynamics of human infections  
  42–9, 43  
  epidemiology in small and large  
  30–3  
positive (+)-sense RNA viruses **75**  
  genomic structure **268**  
  replication 245–71  
  bacteriophages 269–71  
  plant viruses 267–9  
  translation as first step 248  
  viruses with more than one  
  ORF 257–67  
  viruses with one large ORF  
  249–57  
  segmented genomes 258,  
  267–9  
posttranscriptional processing  
  224–6, 226, 227  
  cloned genes 444, 451  
  regulation 231, 231  
  Sindbis virus proteins 262  
  virus-induced changes 232  
  *see also* capping, mRNA;  
  polyadenylation, mRNA;  
  splicing, mRNA  
  *see also* proteolytic processing  
potato spindle tuber viroid 297,  
298  
potato virus Y **268**  
Potexvirus **71**  
Potyviridae **71**  
Poxviridae **71**  
poxviruses 360–5  
  DNA replication 217, 363  
  evolutionary origin 11  
  human **45**  
  mouse model 35–7, 36  
  pathogenesis of disease 364  
  phylogenetic relationships 376,  
  376  
  replication 305, 361–4, 362  
  virion and genome 360–1, 361  
pre-biotic environment 11  
pre-initiation complex 221–2  
pre-integration complex (PIC)  
  388, 389, 400–1  
Pribnow box 220  
primary cells 158–9  
  culture 157, 157  
  immortalization 159–60  
primases 215, 216  
primers  
  viral DNA replication 304  
  *see also* RNA primers  
primosome 216  
prion diseases 13, 54, 298,  
299–300  
prions 13, **29**, 298–300  
probes, nucleic acid 174, 206  
procapsid 92, 92, 254  
productive infections 15, 17, 160  
programmed cell death *see*  
  apoptosis  
progressive multifocal  
  leukoencephalopathy (PML)  
  308, 328  
prokaryotes  
  DNA replication 215, 215–16  
  virus-infected cells 217  
  genome organization 214  
  transcription 219–21  
  translation 234–6, 235  
  *see also* bacteria  
proliferating cell nuclear antigen  
  (PCNA) 216  
promoters  
  cloning plasmids 445  
  eukaryotic 221–3, 222  
  prokaryotic 220  
  SV40 virus 309  
propagation 5  
prophage 372, 375  
prot gene 385  
protease inhibitors 134, 135  
proteases  
  digestion of viral proteins 176  
  maturation 92  
  poliovirus 250, 251–2  
  retrovirus 93, 383  
protein interaction maps (PIMs)  
  479–81, 481, 482  
protein kinase, dsRNA-dependent  
  (PKR) 128, 129, **130**  
proteins  
  cellular surface 80  
  databases 474, 475  
  effects of virus infection on  
  cellular 163–4, 194, 195  
  functional analysis 478  
  integral membrane 80, 81  
  mutated 437–8  
  structural analysis 478  
  structural modeling 478  
  structure database 474  
  synthesis 232–6  
  viral 65, 69, 173–4  
  antigenic structure 102–4,  
  103  
  capsid *see under* capsid(s)  
  characterization in infected  
  cells 193–204  
  denaturation 103, 104, 176  
  immune reagents for studying  
  195–204  
  immunofluorescence methods  
  198–201, 199  
  nonstructural 173–4, 193  
  pulse labeling 194–5, 195  
  size estimates 442  
  structural *see* structural  
  proteins  
  synthesis 232, 236  
  *see also* translation  
proteolytic processing  
  poliovirus proteins 250, 251–2  
  retrovirus proteins 383, 391–2  
proteome 474, 479  
proteosome 106  
proto-oncogenes 392, **393**  
prototrophy 156  
provirus 217, 383  
  HIV-1 404–5  
PrP protein 299  
pseudorabies virus 332  
  entry into cells 85, 86, 340–1,  
  341  
  exit from cells 94, 96  
Pseudoviridae **71**  
PubMed 476

- pUC19 plasmid 445, 446  
 pulse-chase experiments 252  
 pulse labeling, viral proteins  
 194–5, 195  
 Pvr *see* CD155
- Q $\beta$  bacteriophage, replication  
 269, 269–71, 270
- quantal assays 169, 169–70, 170
- quasi-species swarms 248
- R-loop mapping 226–9
- rabbit models, latent HSV infection  
 40
- rabies 8, 29, 30, 55, 280  
 animal models 37, 38  
 control measures 33  
 incubation period 44, 53  
 prodromal period 55  
 vaccine 121–2, 122
- rabies virus 46, 275  
 cellular receptor 80–2  
 Pasteur's studies 121  
 reservoirs 30  
 spread within host 23, 37, 38  
 tissue tropism 23
- Ras protein 394
- rate zonal centrifugation  
 measuring viral genome size  
 185–6  
 viral and cellular DNA  
 separation 205  
 viral structural proteins 174–6,  
 175
- Rb protein 314  
 adenovirus interaction 320  
 EBV interaction 352–3  
 HPV interaction 318  
 SV40 virus interaction 309,  
 311, 313–14
- reactivation (recrudescence) 17,  
 44, 52  
 in animal models 40  
 herpesviruses 333, 348–51,  
 350, 354  
 viruses infecting humans 45–7
- receptor-mediated endocytosis 85,  
 86  
 influenza virus 285, 286  
 poliovirus 253, 253–4  
 SV40 virus 310  
 togaviruses 258–9, 260
- receptors, viral 23  
 animal cells 80–3, 81, 82  
 bacterial cells 87, 88
- recombinant viruses  
 analysis of mutations 439,  
 439–40  
 cloning vectors 449–54  
 generation 456–60, 459–61  
 isolation 456–8, 459–61  
 selectable markers 440–1  
 as therapeutic agents 490–4  
 vaccines 124  
 viral pathogenesis studies 468,  
 469–70
- recombination, genetic 124
- recrudescence *see* reactivation
- regulatory T cells (T<sub>reg</sub>) 107,  
 108–9
- Relenza 134
- Reoviridae 71, 292
- reoviruses 292–5  
 pathogenesis 295  
 replication cycle 294, 294–5  
 structure 292–4, 293
- replica plating 448
- replicase  
 phage Q $\beta$  270, 270–1  
 poliovirus 253, 254
- replication, virus 15–19  
 cell-based defenses against  
 126–31  
 cycle 17–19, 18, 79–80  
 DNA viruses 303–28, 331–57,  
 359–76  
 drugs targeting 131–5, 132  
 dsRNA RNA viruses 292–5  
 hepadnaviruses 413–18  
 negative-sense RNA viruses  
 274–92  
 positive-sense RNA viruses  
 245–71  
 retroviruses 381–97  
 ssDNA viruses 323–6  
 subviral pathogens 295–300
- replication-deficient viruses 453,  
 491
- replication fork 215, 215
- replicative intermediate (RI)  
 ssDNA bacteriophage 326  
 type 1 (RI-1) 246, 247, 247  
 type 2 (RI-2) 246–7, 247
- replicons 11
- reporter genes  
 gene therapy 492, 492  
 pathogenesis studies 468, 468,  
 469–70  
 protein–protein interactions  
 479, 480
- repressors 219, 219, 220–1
- reservoirs 20–1, 27–30  
 human 28  
 vertebrate 30
- resolvase 396
- resource center 501–5
- respiratory infections 49  
 epidemiology 30–1, 31
- respiratory syncytial virus (RSV)  
 47, 281  
 case study 300  
 evasion of immunity 110
- respiratory viruses  
 entry into cells 82  
 transmission 24, 28
- Reston virus 282
- restriction endonucleases 135–6  
 cloning into plasmid vectors  
 445, 447  
 detection of viral DNA in cells  
 205  
 dsDNA size measurement 186,  
 187
- restriction mapping 442–3,  
 443–4
- retrocyclin 2 (RC2) 135
- retroelements 396, 396
- retrointrons 396, 396
- retroposons 396, 396
- retrotransposons 11, 396, 396–7,  
 397
- Retroviridae 71
- retroviruses 47, 381–97  
 budding 94, 95  
 classification 382  
 cloning/expression vectors 452,  
 453  
 complex 382, 386, 399  
 drug therapies 134–5  
 enumeration of virions 153  
 evasion of immunity 111  
 evolutionary origin 417  
 gene therapy vectors 491,  
 492–3  
 genetic maps 386, 387  
 genome 384–6  
 integration into host DNA  
 217, 383, 388, 389,  
 391–2  
 molecular biology 383–6  
 rapid-transforming 386, 392–3  
 related genetic elements 215,  
 395–7  
 replication 246, 386–92, 388  
 capsid assembly and  
 maturation 389, 391–2  
 initiation of infection 386–9  
 mechanism of cDNA synthesis  
 389–91, 390  
 strategies 382–3  
 simple 382, 386  
 slow-transforming 393–5  
 structural proteins 383–4  
 transformation mechanisms  
 392–5  
*rev* gene 400, 401  
 Rev protein 405, 406

- Rev-response element (RRE) 405, 406
- reverse genetics 443
- reverse transcriptase (RT) (Pol) 417
- assays 153
- hepadnavirus (P) 413, 415, 416
- HIV-1 400
- inhibitors 134, 135
- phylogenetic relationships 11
- retrovirus 382, 383
- generation of cDNA 387, 388, 389–91, 390
- synthesis 391–2
- transposable elements 396, 396
- reverse transcription 389–91, 390, 400, 415
- reverse transcription polymerase chain reaction (RT-PCR) 470, 486
- rex* gene 386
- Rhabdoviridae 71, 275
- rhabdoviruses 46
- cytopathology and disease 280
- plant 29
- replication 275–80
- rheumatic fever 109
- rhinoviruses 29, 46, 256
- antigenic drift 110
- entry into cells 84, 84
- replication 249
- Rhizidiovirus* 71
- $\rho$  factor 221
- RI *see* replicative intermediate
- ribavirin 300
- ribonucleases 185–6
- ribonucleic acid *see* RNA
- ribonucleoproteins (RNP) 225
- ribosomal RNA (rRNA) 10, 214
- ribosomes
- arenavirus virions 291
- bacteriophage mRNA translation 269, 270, 270
- eukaryotic translation 233–4, 234
- prokaryotic translation 235, 235–6
- skipping, retroviruses 385, 391
- ribovirin 133
- ribozymes 297
- rice tungro bacilliform virus 416
- Rift Valley fever virus 291
- RIG-1 protein 127
- rimantadine 133–4
- rinderpest 281–2
- RNA 69
- hybridization 205–7, 207
- PCR detection 190
- replication, RNA-directed 246–8, 247
- small 130
- structure 72, 74
- see also* double-stranded RNA; single-stranded RNA; specific types of RNA
- RNA-dependent transcriptase 246, 274
- RNA editing 231, 232
- RNA polymerase
- holoenzyme 219, 220, 220
- phage T7 367
- prokaryotic 219, 220, 221
- T4 modification of *E. coli* 370, 370
- virus-specific 232
- RNA polymerase II (pol II) 221–2
- hepatitis delta virus replication 297
- SV40 virus replication 311
- RNA polymerase III (pol III), VA
- RNA transcription 319, 323
- RNA primers
- DNA replication 215, 216
- DNA viruses not using 304
- retroviral cDNA synthesis 389
- viral DNA replication 304
- RNA viruses 69, 246
- classification 75, 246
- detection of genome synthesis 205
- with dsRNA genomes 246, 292–5
- evasion of immunity 110
- genome sequencing 180–1
- inhibition of host transcription 232
- negative (–)-sense *see* negative (–)-sense RNA viruses
- positive (+)-sense *see* positive (+)-sense RNA viruses
- structure and size 68
- see also* retroviruses
- RNase-H 389–91, 390, 415
- RNase-L 128, 130
- rolling circle replication 344, 345, 369, 369
- roseola 332
- rotaviruses 292, 295
- vaccine 122
- Rous sarcoma virus (RSV) 308, 393
- genetic map 386, 387
- routes of inoculation 466, 466–7, 467
- routes of transmission 28, 29
- RT-PCR *see* reverse transcription polymerase chain reaction
- R:U5:(PBS):leader region 385
- rubella 29, 263
- congenital/fetal 50, 110, 263
- vaccine 122
- rubella virus 47, 263
- Rubulavirus* *see* mumps, virus
- Rudiviridae 71
- s* value 176, 186
- S<sub>1</sub>-nuclease 229–30
- Sabin poliovirus vaccine 122, 126
- v-sag* gene 386
- Salk poliovirus vaccine 123
- Sanger technique, DNA sequencing 182, 183–4
- SARS *see* severe acute respiratory syndrome
- SARS coronavirus (SARS-CoV) 27, 31, 46, 267
- replication 265–6
- scaffolding proteins 80, 92, 92–3
- scale-free networks 479, 480
- SCID-hu mouse 464–5
- scrapie 13, 298, 299
- screening
- mutant viruses 439, 441
- recombinant plasmids 445
- sedimentation constant (*s* value) 176, 186
- segmented genomes
- dsRNA RNA viruses 294, 295
- negative-sense RNA viruses 274, 283–92
- plant DNA viruses 325
- positive-sense RNA viruses 258, 267–9
- selectable genetic markers 445
- selection, mutant viruses 439, 440–1
- selfish genes 3–4
- Semliki Forest virus expression vector 454, 455
- Sendai virus 280, 281
- senescence, cultured cells 158, 159
- sequence analysis
- bioinformatics tools 478
- viral genomes 180–4, 182
- sequence similarity searching tools 476, 477
- Sequiviridae 71
- serotypes 110
- Serratia marcescens* 489–90

- severe acute respiratory syndrome (SARS) 48, 267  
 epidemiology 31–3, 32  
 virus *see* SARS coronavirus
- severe combined immunodeficient (SCID)-hu mouse model 464–5
- sex pili 87
- shapes, virus 69–72
- Shine–Dalgarno sequence 235, 235
- shingles 52, 332
- sialic acid residues 82, **82**
- signal transduction 81, 223–4
- simian immunodeficiency virus (SIV) 399–400
- simian sarcoma virus **393**
- simian vacuolating agent 40 *see* SV40 virus
- similarity searching tools 476
- Sin Nombre virus **29**, 291
- Sindbis virus 163, 258–62, **268**  
 genome 258, 259  
 replication cycle 258–62, 260, 261–2
- single-stranded DNA (ssDNA)  
 adenovirus DNA replication 321, 322  
 binding proteins 218  
 cloning with bacteriophage M13 451  
 restriction mapping 442–3  
 size measurement 186  
 viruses, replication 305, 323–6
- single-stranded RNA (ssRNA)  
 measuring size 185–6  
 replication of genomic 246–8, 247  
 restriction mapping 442–3
- Siphoviridae **71**
- Sis protein 394
- size, virus 65, 66
- small interfering RNAs (siRNAs) 130, 214
- small nuclear RNA (snRNA) 225
- small t antigen 309, 311, 312
- smallest self-replicating pathogens 13  
*see also* subviral infectious agents
- smallpox (variola) **29**, 48, 49–50  
 animal models 36  
 eradication 33, 121, 365  
 history of vaccination 120–2  
 impact on human history 8  
 major and minor 49, 120, 364  
 pathogenesis 364  
 vaccine 121, 122, **122**, 365
- smallpox (variola) virus **45**, 49–50
- bioterrorism threat 364–5, 489  
 genome 360  
 persistence in environment 27
- SNDV-like viruses **71**
- Sobemovirus* **71**
- sodium dodecyl sulfate (SDS)  
 denaturing gel  
 electrophoresis 176–7, 177
- SOS repair system 375
- Southern blot 202
- Spanish influenza epidemic (1918–19) 8, 48, 49, 190, 486, 486
- spliceosomes 225
- splicing, mRNA 225–6, 227, 231  
 adenovirus 228–30, 319, 320, 321  
 HIV-1 405  
 influenza virus 284, 286  
 patterns used by viruses 228–30  
 retroviruses 391, 392  
 SV40 virus 306–7, 309, 310, 312  
 virus-induced changes 232  
 visualizing and localizing 226–31
- spumaviruses 382
- v-src* oncogene 386, 387
- Src proteins 394
- ssDNA *see* single-stranded DNA
- ssRNA *see* single-stranded RNA
- St Louis encephalitis virus 256
- staphylococcal A protein 201–2, 202–3, 203–4
- statistical analysis of infection 168
- stop codons *see* termination codons
- streptococcal G protein 201–2
- stress, HSV reactivation 348, 351
- strong stop 391
- structural analysis 478
- Structural Classification of Proteins (SCOP) 475
- structural modeling 478
- structural proteins 65, 173–9  
 isolation 174–6  
 size fractionation 176–9, 177  
 stoichiometric analysis 177–8, 178
- structure, virus 65–72, 67–8, 73, 74
- subacute sclerosing panencephalitis (SSPE) 53, 109
- subcutaneous inoculation 35, 36
- subgenomic mRNA  
 negative-sense RNA viruses 284, 286, 289–90, 292  
 plant RNA viruses 268, 269
- positive-sense RNA viruses 261, 261, 263–4, 265, 266
- subviral pathogens 297  
*see also* segmented genomes
- subunit vaccines 124–5
- subviral infectious agents 13, 65  
 replication 295–300  
*see also* defective virus particles; prions; viroids
- sucrose density gradients 174, 175  
*see also* rate zonal centrifugation
- superfamilies 77
- suppressible stop codons 236  
 bacteriophage Q $\beta$  270  
 retrovirus 385, 391  
 Sindbis virus 259, 259
- SV40 virus  
 abortive infection 312–14  
 entry into cells 83, 84, 310–12  
 genome and genetic map 306–7, 309–10, 441  
 polio vaccine contamination 123–4  
 productive infection 310–12  
 replication 305–14, 311, 313  
*see also* large T antigen; small t antigen
- symmetry, virus 69–72
- symptoms, disease 23–4
- syncytia 83, 163
- syphilis, Tuskegee studies 34
- systems biology 479–81
- T antigen *see* large T antigen
- t antigen *see* small t antigen
- T cells *see* T lymphocytes
- T helper 1 cells (Th1) 101–2
- T helper 2 cells (Th2) 101–2
- T lymphocytes 100–1, 102  
 antigen presentation to 106  
 clonal selection 107  
 effector 24, 106, 107  
 HIV infection 22, 82, 106, 407–8  
 measurement of response 112  
 memory 108  
 regulatory (T<sub>reg</sub>) 107, 108–9  
 viruses infecting **22**  
*see also* CD4<sup>+</sup> T cells; CD8<sup>+</sup> T cells; cytotoxic T lymphocytes; helper T cells
- T1 bacteriophage **88**
- T2 bacteriophage **88**
- T4 bacteriophage 367–70  
 capsid maturation and release 370, 371  
 DNA ligase 445  
 entry into *E. coli* 87–9, **88**, 88

- genome extrusion 179, 181  
 genome structure 368, 368–9  
 replication 369, 369–70, 370  
 T5 bacteriophage **88**  
 T6 bacteriophage **88**  
 T7 bacteriophage 365–7, 366  
 Tamiflu 134  
 TAPs 106  
 target tissues/organs 22  
   damage to “accidental” 50  
   viruses with specific 54–8  
*tat* gene 400, 401  
 Tat protein 405  
 TATA box 220, 221–2, 222  
   SV40 virus 309  
 TATGARAT sequence 341, 342  
*tax* gene 386  
 TCID<sub>50</sub> 169  
 Tectiviridae 71  
 tegument 334  
 telomerase 217, 304, 352–3, 382  
 telomeres 159, 217  
 temperature-sensitive (*ts*) mutations  
   161, 439, 439–40  
*Tenuivirus* 71  
 termination codons, translation  
   233  
   mutations involving 437, 438  
   skipping, retroviruses 385, 391  
   suppressible *see* suppressible stop  
   codons  
 termination factor ( $\rho$  factor) 221  
 tetracycline resistance marker 445,  
   448–9  
 Tetraviridae 71  
 therapeutic index 131  
 therapeutic uses of viruses 490–4  
   destruction of other viruses 493  
   nanotechnology 493–4  
   vectors for gene delivery **491**,  
   491–3  
 thymidine kinase (TK) 132,  
   440–1  
 tick-borne encephalitis, vaccine  
   **122**  
 $\alpha$ -TIF protein 340, 341–3, 342  
 tissue culture infectious dose,  
   median (TCID<sub>50</sub>) 169  
 tissue tropism 23, 54, 80–3  
 titers, virus 166–8  
 tobacco mosaic virus (TMV) 267,  
   **268**  
   assay 165  
   capsid assembly 89–91, 91  
   nanotechnology applications  
   494  
   replication 268  
 tobacco rattle virus **268**  
*Tobamovirus* 71  
*Tobravirus* 71  
 Togaviridae 71  
 togaviruses 46–7, 258–63  
   cloning/expression vectors **452**,  
   454, 455  
   cytopathology and disease  
   262–3  
   genome 258, 259  
   replication cycle 258–62, 260,  
   261–2  
 Toll-like receptors (TLR) 99, 102  
 tomato bushy stunt virus 268,  
   **268**  
 tomato golden mosaic virus 326  
 tomato spotted wilt virus **29**, 85  
 Tombusviridae 71  
 topoisomerases 312, 313  
 toroviruses 263  
*Tospovirus* **289**  
 tospoviruses 290  
 Totiviridae 71  
*trans*-acting genetic elements 214  
*trans*-activating response element  
   (TAR) 405, 405  
 transcriptase, RNA-dependent  
   246, 274  
 transcription 214, 217–32  
   discontinuous negative-strand  
   265, 266  
   DNA bacteriophages 367, 370,  
   372–5  
   eukaryotic 221–32  
   control of initiation 223–4,  
   224  
   initiation 221–3, 222, 223  
   hepadnavirus 415  
   HIV-1 405, 405  
   integrated retroviral cDNA  
   389, 391  
   latent herpesvirus infections  
   342, 348–9  
   leader-primed 265, 266  
   negative-sense RNA viruses  
   276, 284, 285, 286, 289,  
   292  
   poxviruses 363, 364  
   productive herpesvirus infections  
   341–3, 342  
   prokaryotic 219–21  
   control of initiation 220–1  
   initiation 220  
   termination 221  
   reverse 389–91, 390, 400, 415  
   RNA viruses replicating without  
   248  
   RNA viruses requiring 274  
   RNA viruses with dsRNA  
   genomes 294  
   subviral pathogens 297  
   SV40 virus 306–7, 309–10,  
   311  
   virus-induced changes 232  
   *see also* posttranscriptional  
   processing  
   transcription factors 222, 223  
   herpesvirus 341–3  
   transcription-termination signals  
   225  
   transcription/translation, coupled  
   235  
 transcriptome 474, 479  
 transfection 89, 90  
   bacterial plasmids 445  
 transfer blots 202  
 transfer RNA (tRNA) 214  
   plant RNA viruses 267  
   translation initiator 233, 235  
 transfer vector 452  
 transformation 17, 159–60, 160  
   adenovirus-mediated 323  
   bacterial 445  
   focus of 166, 166, 314  
   herpesvirus-induced 354  
   retrovirus-mediated 392–5  
   SV40-induced 314  
   transitory (abortive) 314, 315  
 transformed cell foci 165–6, 166  
 transgenic mice 464, 465  
   bioluminescent imaging 468–9,  
   469  
   immune responses 471  
 transgenic plants, edible vaccines  
   125  
 translation 214, 232–6  
   eukaryotic 233–4, 234  
   as first step in RNA virus  
   expression 248  
   in vitro 209, 210  
   negative-sense RNA viruses  
   285, 286, 289–90  
   plant RNA viruses 267, 268,  
   269  
   positive-sense RNA viruses  
   with multiple ORFs 257–8,  
   259, 260, 266  
   with one large ORF 249–51,  
   250, 257  
   prokaryotic 234–6, 235  
   retrovirus mRNA 385–6, 391,  
   392  
   RNA bacteriophage mRNA  
   269, 269–71, 270  
   virus-induced changes 236  
 translocation 83–4  
 transmission, virus 24  
   modes of 28  
   routes of 28, **29**  
 transposase gene 395–6

- transposons **395**, 395–6, 397  
*Trichovirus* **71**  
 tRNA *see* transfer RNA  
 tropism, tissue *see* tissue tropism  
 tumor antigens 100  
 tumor suppressor genes 52, 164  
*see also* p53 protein; Rb protein  
 tumors  
   cell culture 159  
   induction by viruses 160  
   polyomavirus-induced 308,  
     314–16, 318  
   retrovirus-induced 386, 392–5  
*see also* cancer  
 Tuskegee syphilis studies 34  
 Ty1 retrotransposon 396, 397  
*Tymovirus* **71**
- ubiquitins 106  
*Umbrovirus* **71**  
 uncoating, partial  
   HIV-1 400, 403  
   poxvirus 363  
 UniProt 474  
 Universal Virus Database  
   (ICTVdB) **483**
- VA RNA 319, 321–3  
 vaccination 5, 33, 120–6  
 vaccines 120, **122**  
   capsid and subunit 124–5  
   DNA 125  
   edible 125  
   Jennerian 122  
   killed-virus 123–4  
   live-virus 122–3  
   problems with 125–6  
   production 122–5  
   recombinant virus 124  
   storage 123, 126  
 vaccinia virus  
   as cloning/expression vector  
     452, **452**  
   receptor 23  
   recombinant vaccines 124  
   replication 361–4, 362  
   smallpox vaccine 122  
   virion and genome 360, 361  
 varicella zoster virus (VZV) **29**,  
**45**, 332  
   gene transfection 89, 90  
   protein localization methods  
     200–1, 200–1  
   reactivation 52
- transmission 24, 28  
*Varicosavirus* **71**  
 variola *see* smallpox  
 variolation 121  
 vectors 20, 28, **29**, 30  
   cloning *see* cloning vectors  
   encephalitis viruses 56  
   new geographic ranges 488,  
     489  
   plant viruses 85, 326  
 vegetative DNA replication  
   343–4, 345  
 Vero cells 165, 167  
 vesicular stomatitis virus (VSV) **8**,  
 275–80  
   cytopathology and disease 280  
   defective interfering (DI)  
     particles 454  
   HIV-directed recombinant  
     493  
   interferon-induced defenses  
     128  
   mechanisms of host shutoff  
     279–80  
   plaque assays 130  
   replication 275–80, 277–8,  
     279  
   virion and genome 275, 276  
 VIDA 475, 478, **483**  
*vif* gene 400, 401  
 Vif protein 401–4, 404  
 Viral Bioinformatics Resource  
   Center **483**, 505  
 viremia 22  
 virions (virus particles) 65  
   assembly 80, 89–93  
   enumeration 149–51, 152–3  
   envelope generation 93–4  
   exit from cells 93–4, 95  
   fractionation 174–7, 177  
   isolation 174, 175  
   visualization 147–53  
 viroids 13, 297–8, 298  
 VirOligo **483**  
 virology 3–13  
   books 501–2  
   history 7–9  
   internet resources 504–5  
   journals 503  
   reason for studying 494  
 virosphere 77, 78  
 virulence 5  
   assays 466–7  
   attenuation 121, 122–3
- reversion to, vaccines 123  
 virus(es)  
   constructive impact on society  
     12–13  
   features 65–72  
   living/nonliving nature 3–4  
   numbers of different types 65  
   origin 9–11  
   size 65, 66, 67–8  
 virus–host interactions 6–7  
   classification of viruses by  
     44–9  
   dynamics 42–9  
   evolutionary impact 9  
   techniques of studying 34–5  
 Virus Database (VIDA) 475, 478,  
**483**  
 virus particles *see* virions  
*Vitivirus* **71**  
*vpr* gene 400, 401  
 Vpr protein 400, 406  
*vpu* gene 400, 401  
 Vpu protein 405–6, 407  
 VSV *see* vesicular stomatitis virus  
 VZV *see* varicella zoster virus
- warts 52, 314  
   formation 316–18, 317  
   transmission 28  
 wasps, parasitic 9, 111  
 Watson–Crick base-pairing rules  
   215, 217  
 West Nile virus **46**, 48, 256,  
 488–9  
   DNA vaccine 125  
 western blot 202, 202–3  
 Western equine encephalitis **29**  
 World Health Organization  
   (WHO) 125–6, 490  
 wound tumor virus 292
- x-ray crystallography 72, 73, 74,  
 151
- yeast  
   retrotransposons 396, 397  
   two-hybrid detection system  
     479–81, 480  
 yellow fever **29**, **46**  
   vaccine **122**  
   virus 257, 257, **268**
- zoonoses 27–8, 28, 30  
   patterns of infection 48–9