

# Index

Page references followed by f denote figures, those followed by t denote tables.

## A

- AAA<sup>+</sup> ATPases, 155
- AbaSI, 246
- Acinetobacter baumannii*, 246
- ACNs (anticodon nucleases), 230
- AcuI, 129, 130t, 322
- Adamczyk-Poplawska, Monika, 252
- Adenosine triphosphate. *See* ATP
- Adenovirus, split genes in, 49
- AFM. *See* Atomic force microscopy (AFM)
- Agarose slab gel electrophoresis, 52, 66
- AgeI, 194t
- Aggarwal, Aneel, 79, 128, 134, 138, 205, 236, 238, 241
- AhdI, 130t
  - control by C proteins, 213
  - recent studies, 294t
  - recognition sequence, 294t
- Alkyladenine glycosylase, 243f
- Allelism, of R-M genes, 21–23
- Alol, 195
- Ames test, 13
- Anderson, John, 96
- Anticodon nucleases (ACNs), 230
- Antirestriction, 230–232, 234–235
- Anti-restriction-modification (anti-RM) systems, 230, 235
- Antisense RNA, 214
- ApeKI, 322
- Apoptotic mutual exclusion, 214
- Applications of restriction enzymes, modern-day, 317–306
- Apyrimidine lyase, 319
- Arber, Werner, 228
  - Arber-Dussoix papers, 17–19
  - Bertani and, 14
  - DNA modification, 20–21
  - E. coli* B REase, 20
  - Edouard Kellenberger and, 35
  - Hamilton Smith and, 39
  - host-controlled variation, 1, 6, 8, 15, 17–19
  - journal club seminar on Watson and Crick model of DNA, 15–17
  - models for hyphenated and/or palindromic recognition sites, 22–23
  - Nobel Prize, 1, 6, 33, 35, 40
  - PhD thesis, 16f, 17
  - photograph, 16f, 50f, 199f
  - Thomas Bickle and, 42
  - transduction by lambda, 12–13
- Archaea, 125
- ArdA, 223–224, 231–232
  - effectiveness of inhibition of Type I R-M systems, 234–235
  - structure, 233, 234f
- ArdB, 231–232
  - effectiveness of inhibition of Type I R-M systems, 234–235
  - structure, 233–234, 234f
- Argonaute proteins, 325
- AS1 (Aggravated Sludge 1) bacterial strain, 88
- AspBHI, 247
- AspCNI
  - catalytic domains, 193
  - recent studies, 294t
  - recognition sequence, 294t
- ATAC-seq, 324–325
- Atomic force microscopy (AFM), 158
  - Type I restriction enzymes, 216, 224
  - Type IIE restriction enzymes, 196, 198
- ATP
  - DNA translocation and, 155–156, 158–159, 227, 253
  - EcoKI DNA cleavage and, 108
  - restriction enzyme requirement for, 30–32, 34, 43, 78, 104
  - Type III enzymes and, 111, 236, 238, 240–241, 253, 307
- AvaI, 43
- Avery, Oswald, 16

## B

- Bacillus*
  - B. amlioliquefaciens*, 134
  - B. stearothermophilus*, 142
  - B. subtilis*
    - restriction enzymes, 43
    - subsp. globigii, 134
- BspLU11III, 202
- m<sup>4</sup>C modification, 187
- Balendiran, Ganesaratnam, 213
- BamHI
  - altering specificity, 127
  - BamHI–DNA complex, 135, 136f
  - cloning of, 55, 134
  - control of restriction, 211, 213
  - crystal structure, 96–97, 96f
  - DNA binding, 91, 92
  - DNA cleavage, 71
  - DNA interactions, 132
  - recognition sequence, 53, 53f, 205
  - restriction folds, 146f
  - specificity, 138

- BamHI (*Continued*)  
stable DNA–protein complexes  
in absence of Mg<sup>2+</sup>, 91  
structure, 103, 127–128, 134–135, 136f, 146, 186  
Barrier to infection, discovery of, 5–8  
Base analogs, affect on DNA cleavage of, 100  
Base flipping, 3, 128, 186  
by MspJI, 246  
by PabI, 207  
Bases, modified, 186–187  
BbsI, 319  
BbvCI, 207  
recent studies, 294t  
recognition sequence, 188, 294t  
BcgI, 42–43, 88, 90, 129, 130t  
DNA cleavage, 195  
recent studies, 294t  
recognition sequence, 195, 294t  
structure, 129  
BcnI  
DNA cleavage mechanism, 204  
recent studies, 294t  
recognition sequence, 204, 294t  
subunit/domain composition and cleavage  
mechanisms, 200  
B-DNA, 132, 186, 240  
Beadle, George, 17  
Benner, Jack, 56  
Berg, Paul, 19, 87  
Bertani, Elizabeth, 10, 14, 17  
Bertani, Giuseppe (Joe)  
Arber and, 15, 17  
host controlled variation, 5–8, 6f, 10–12, 14  
letter to Noreen Murray, 10–13  
obituary, 13–14  
phage P1 and, 17–18, 77  
BfiI, 150  
catalytic domain, 191, 193  
reaction mechanism, 147  
recent studies, 294t  
recognition sequence, 294t  
BglII, 127, 129, 130t, 147  
BglIII  
cloning of, 55, 134  
control by C proteins, 213  
DNA interactions, 136f, 137  
recognition sequence, 205  
specificity, 138  
structure, 127–128, 134, 136f, 137  
Bickle, Thomas, 42, 231  
genetic selection operating at population  
level, 112, 149  
Type I restriction enzymes, 75  
Type III restriction enzymes, 79  
BioBrick, 318, 319  
BisI  
recent studies, 295t  
recognition sequence, 204, 295t  
Bitinaite, Jurate, 57f  
BlnI, 188  
Blumenthal, Bob, 187, 211  
*Bordetella pertussis*, 231, 233  
Boyd, Chris, 88  
Boyer, Herbert, 311f  
EcoBI purification, 24  
EcoRI discovery, 21, 36, 40–41  
PhD thesis, 40–41  
Bpu10I, 129, 130t, 188  
BpuSI, 228, 229f  
methylation, 202  
recent studies, 295t  
recognition sequence, 196, 203, 295t  
subunit/domain composition and cleavage  
mechanisms, 203  
Brammar, William, 52  
Chris Boyd and, 88  
EcoKI genes, cloning of, 54  
Brooks, Joan, 55  
Brown, Nigel, 69  
BsaI, 319, 320f  
BsaI-HF v2, 319, 320f  
BsaWI, 194t  
BsaXI  
recent studies, 295t  
recognition sequence, 195, 295t  
subdomains, 195–196  
Bse634I, 142, 143f, 144  
CCGG family of restriction enzymes, 194t  
recent studies, 295t  
recognition sequence, 200, 295t  
subunit/domain composition and cleavage  
mechanisms, 200  
BseRI, 202  
BslI, 129, 130t  
BsmBI, 319  
BsmFI, 321  
BsoBI, 127  
BspD6I  
recent studies, 295t  
recognition sequence, 295t  
BspI, 71  
BspLU11III, 202  
BspMI, 159  
recent studies, 295t  
recognition sequence, 295t  
BspRI  
recent studies, 295t  
recognition sequence, 295t  
BssHIII, 323  
Bst DNA polymerase, 323–324  
BstNI, 138–139  
BstYI  
recent studies, 295t  
recognition sequence, 205, 295t  
structure, 205  
Bsu36I, 188  
BsuRI  
molecular weight, 91  
recognition sequence, 188  
Bucci, Pat, 40  
Bujnicki, Janusz, 128  
Bullas, Len, 104  
Burns, Ken, 39f  
Butkus, Viktoras, 57f

## C

3C (chromosome conformation capture)-based technologies, 324  
C (control) proteins, 187, 212–214, 212f, 307  
Ca<sup>2+</sup>, 191  
Call, 71  
Campbell, Allan, 12  
*Campylobacter jejuni*, 249  
Cas9 fusions, 209  
Catenane assays, 140, 141f, 142  
CCGG family of restriction enzymes, 193, 194t  
CCGG group photo, 198f  
CCR5, 152  
Cfr91, 91, 93  
Cfr101  
    CCGG family of restriction enzymes, 194, 194t  
    recent studies, 295t  
    recognition sequence, 186, 194, 194t, 200, 295t  
    restriction folds, 146f  
    structural localization of active site residues, 145f  
    structure and biochemistry, 141–142, 143f, 144  
Cfr421, 201  
CglI  
    recent studies, 296t  
    recognition sequence, 296t  
Chan, Siuhong, 317  
Chandrasegaran, Srinivasan, 152, 208  
Chargaff, Erwin, 16  
Chimeric restriction enzymes, 127, 151–152  
ChIP-based sequencing, 322  
Chromatin  
    mapping of open chromatin regions, 324–325  
    spatial structure, study of, 324  
Chromosome conformation capture (3C)-based technologies, 324  
Circular permutations, 3, 129, 215  
*Citrobacter freundii*, 103, 142  
Cjel, 195  
Clamp loader, 240  
Clark, John, 31  
Cleavage. *See* DNA cleavage  
Cloning vectors, EcoRI, 41  
ClpXP  
    proteolysis mediated by, 230, 307  
    restriction alleviation, 161, 161f  
Co<sup>2+</sup>, 188, 191  
Codon usage in R-M systems, 125  
Coevolution, 153  
Collision model for DNA breakage, 108–109, 109f, 158–160, 160f, 307  
Comb, Don, 53  
Commercially available restriction enzymes in 1970s, 65, 66f  
Control of restriction, 187, 211–215, 212f, 307  
Control (C) proteins, 187, 212–214, 212f, 307  
Convergent evolution, 188, 201  
CpG islands, demethylation of, 232  
CRISPR, 152, 252, 306, 325  
Crossing-over, evolution of DNA specificity of Type I enzymes by unequal, 105, 307

Crystallography of Type II restriction enzymes, 95–99, 131, 188  
Csp2311, 214  
Cu<sup>2+</sup>, 188, 205  
CUTTER, 53  
Cuvier, Georges, 43  
Cys4-Zn<sup>2+</sup>, 191  
Cytosine epigenetic markers, mapping, 323

## D

Dam methyltransferase, 67–68, 72, 251  
Danna, Kathleen, 321  
Dcm, 244  
DdeI, cloning of, 55  
DEAD box motif, 155–157  
DeepSAGE, 321  
Delbrück, Max, 6, 13–15  
Demerec, Milislav, 13  
*Desulfococcus oleovorans*, 215  
Dickerson, Richardson, 69  
Divergent evolution, 188  
DNA assembly technologies, in vitro, 318  
DNA binding by Type II restriction enzymes, 91–93, 92f, 93f  
DNA cleavage. *See also specific enzymes*  
    BamHI, 135  
    diversity in, 126  
    metal ions and, 150–151  
    models for Type I restriction enzymes, 108–109  
    phosphorothioates, affect of, 100–101  
    restriction enzymes needing two copies of recognition sequence, 126, 129  
    as two-step process  
        Type II restriction enzymes, 70–71, 93–94  
        Type III restriction enzymes, 111–112  
DNA fingerprinting, 255, 255f  
DNA glycosylase, 207  
DNA helicases, 155  
DNA inactivation by restriction, 17–19  
DNA libraries, 321–322  
DNA ligase, 54, 95, 317, 321, 322f  
DNA looping, 126, 140, 141f, 142, 226f, 237–238  
DNA mapping, 44, 321  
DNA methylation. *See* Methylation  
DNA modification. *See also* Methylation  
    Arber-Dussoix paper, 19  
    discovery of, 186  
    mapping epigenetic modification, 323  
    role of methionine in, 20–21  
    Type IV restriction enzyme dependence on, 186, 241–247  
DNA recognition functions of Type II restriction enzymes, 99–101  
DNA replication, semiconservative nature of, 16  
DNA sequencing, restriction enzyme use in, 44  
DNA specificity. *See* Specificity  
DnaB, 229  
DnaE, 229  
DNA–protein interfaces of Type II restriction enzymes, 99

- DNase I-based sequencing methods, 324–325  
DNase-Seq, 324–325  
Doermann, Gus, 13  
Double digests, 57  
DpnI, 129, 130t  
  methyltransferase, 89  
  recent studies, 296t  
  recognition sequence, 204, 296t  
  subunit/domain composition and cleavage mechanisms, 204  
DpnII  
  3C-based methods and, 324  
  methyltransferase, 89  
  recognition sequence, 204  
Drug resistance, 28, 41  
Dryden, David, 220, 226, 235  
Dussoix, Daisy. *See* Roullan-Dussoix, Daisy
- E**
- EagI, 323  
Ecl18kI, 199  
  CCGG family of restriction enzymes, 194t  
  recent studies, 296t  
  recognition sequence, 199, 296t  
EcoAI, 161  
  circular permutation of HsdS, 215  
  methylation, 110  
EcoBI (EcoB), 103, 305  
  classification as Type IA enzyme, 104  
  DNA cleavage, 108  
  methylation, 110  
  purification, 24–25  
  reaction mechanism, 77  
  recognition sequence, 76  
EcoBI methyltransferase (MTase), 25  
EcoDXXI, 107  
Eco57I, 88, 129, 130t  
  recent studies, 296t  
  recognition sequence, 196, 202, 296t  
  subunit/domain composition and cleavage mechanisms, 202  
Eco72I, 213  
Eco29kI  
  GIY-YIG motif, 191  
  recent studies, 296t  
  recognition sequence, 191, 296t  
EcoKI (EcoK), 18–19, 305  
  ATP as allosteric effector, 253  
  classification as Type IA enzyme, 104  
  cloning of genes encoding, 54, 55  
  DNA cleavage, 108–109  
  DNA translocation, 155–156, 157f, 158–159, 216–217  
  enzyme structure and mechanisms, 108  
  HsdM protein, 153, 154f  
  HsdR protein, 153, 154f, 225f, 226–228  
  HsdS protein, 153, 154f  
  M-EcoKI (M2S1) complex, 217–220, 218f–219f  
  methylation, 110, 309  
  methyltransferases, 217, 218f, 255–256  
  modeling DNA recognition complex of EcoKI trimeric complex, 153–155, 154f  
  nomenclature, 103  
  purification, 23–24, 24–25, 29–34  
  reaction mechanisms, 76–77  
  recent studies, 302t  
  recognition sequence, 76, 302t  
  R2M2S1 complexes, 220–228  
  S-adenosylmethionine (SAM) and, 153, 255  
  single-molecule studies, 216–217  
  structure, 154, 221f, 224, 225f, 307  
  subunits of, 108  
  translocation, 307  
EcoP1I (EcoP1), 5, 18, 77–78, 110  
  genetics of, 78  
  *mod* gene, 111  
  purification, 78  
  reaction mechanism, 111  
  recognition sequence, 78, 111  
  *res* gene, 111  
EcoP15I (EcoP15), 77, 110, 236–241  
  DNA cleavage, 112  
  DNA recognition by, 238  
  genetics of, 78  
  Huntington's disease and, 206  
  *mod* gene, 111  
  reaction mechanism, 111  
  recent studies, 303t  
  recognition sequence, 78, 111, 303t  
  *res* gene, 111  
  restriction by, 240–241  
  structure, 237–241, 239f, 253, 307  
  structure of EcoP15I/DNA/AMP complex, 238, 239f  
  in SupersAGE and DeepSAGE, 321  
  translocation, 253  
*Ecaprrl* system, 230  
EcoRI, 129, 130t, 305  
  action of, 88  
  altering specificity, 127  
  biochemistry of, 68, 132  
  3C and, 324  
  dimer, 143f  
  discovery of, 21, 36, 40–41, 65  
  DNA binding, 91–93  
  DNA cleavage, 99, 204, 205  
  DNA interactions of, 73–74, 132  
  DNA recognition, 99–101  
  DNA–protein interfaces, 99  
  fidelity of, 71  
  genes  
    cloning of, 54  
    DNA sequence of, 68  
    organization, 91  
  homodimer, 68  
  lambda mutants with variation in number of EcoRI sites, 69–70, 70f  
  operon, regulation of, 205  
  organization, genes and, 91  
  purification, 68–70

- recent studies, 296t
- recognition sequence, 41, 88–89, 144, 185, 188, 296t
- restriction folds, 146f
- RNA–DNA hybrids, cleavage of, 72
- RsrI similarity to, 188
- specificity, 95, 101, 132
- stable DNA–protein complexes in
  - absence of Mg<sup>2+</sup>, 91
- star (\*) activity, 95, 205
- structural localization of active site residues, 145f
- structure, 95–99, 96f, 103, 131–132, 143f, 145–147, 145f
- target site location, 93
- transcriptional control of restriction, 214
- as Type IIP restriction enzyme, 43
- water role in recognition, 149
- EcoR124I (EcoR124), 104–105, 106f, 107, 161, 251–252
  - DNA translocation, 226f
  - HsdM protein, 224, 225f–226f
  - HsdR protein, 222–224, 222f, 225f–226f
  - HsdS protein, 108, 224, 225f–226f
  - recent studies, 302t
  - recognition sequence, 302t
  - R2M2S1 complexes, 220–228
  - R1M2S1 form of, 228
  - single-molecule studies, 216–217
  - structure, 221f, 224, 225f
- EcoRI methyltransferase, 68
  - DNA contacts made by, 74
  - monomeric, 68
- EcoRI–DNA enzyme complex, structure of, 97–99, 98f
- EcoRII, 41, 88, 129, 130t
  - activation in *trans*, 138–139, 139f
  - CCGG family of restriction enzymes, 193–194, 194t
  - cloning of genes encoding, 54
  - DNA cleavage, 94
  - genes and organization, 91
  - PD...(D/E)XK motif, 149
  - recent studies, 297t
  - recognition sequence, 65, 90, 138, 142, 193–194, 194t, 297t
  - refractory sites, 128
  - satellite DNA cleavage, 45
  - stable DNA–protein complexes in
    - absence of Mg<sup>2+</sup>, 91
  - subunit/domain composition and cleavage mechanisms, 196, 197f, 198–200
  - translocation along DNA, 199
- EcoR124II (EcoR124/3), 105, 106f, 107, 251–252
- EcoRII-C, 199
- EcoR124I–Ocr complex, 223
- EcoRV, 65, 87, 127, 129
  - action of, 88
  - altering specificity, 127
  - cloning of genes encoding, 54
  - control by C proteins, 213
  - crystal structure, 96–99, 96f
  - DNA binding, 91–93, 92f
  - DNA cleavage, 94, 99, 132, 204
  - DNA interactions, 134
  - DNA recognition, 100–101
  - DNA–protein interfaces, 99
  - metal cofactors, 150–151
  - recent studies, 297t
  - recognition sequence, 297t
  - restriction folds, 146f
  - sliding along DNA, 204–205
  - specificity, 95
  - stable DNA–protein complexes in
    - absence of Mg<sup>2+</sup>, 91
  - structure, 103, 132–134, 133f, 145–147, 186
- EcoRV–DNA enzyme complex, structure of, 97–99
- Eisenstark, Abe, 6f
- Endonuclease R, purification of, 49
- Endonuclease structural domains, 191–193
- Endonuclease Z, 49
- Endonucleases, homing, 191, 208, 210f, 325
- EndoR. *See* HindII
- Enterococcus faecalis*, 231, 233
- “Epigenetic identity,” 214
- Epigenetic modification, mapping, 323
- Epigenetics, 21, 186
- Escherichia coli*
  - CFI073, 231, 233
  - CT596, 241
  - Type I enzymes from, 103
- Esp3I, 89, 319
- Esp1396I, 212f, 213
- Eubacteria, 125
- Evolution, 54, 190
  - antirestriction, 231
  - convergent, 188, 201
  - divergent, 188
  - DNA specificity of Type I restriction enzymes, 104–107, 106f, 307
    - by homologous recombination within the *hsdS* gene, 104–105, 106f
    - by transposition within the *hsdS* gene, 107
    - by unequal crossing-over within the *hsdS* gene, 105, 106f, 107
  - independent by most restriction enzymes, 91
  - neutral drift, 188
  - PD...(D/E)XK motif family of restriction enzymes, 145–147, 185
  - relationship between restriction enzymes, 148–149, 148f
  - slipped-strand mispairing (SSM), 247
  - Type I R–M systems, 153, 307
  - Type IIF restriction enzymes, 144
  - Type IIG enzymes from Type I enzyme, 228, 229f
- Evolutionary trees, 2, 128
- Exonuclease-based DNA assembly methods, 320–321, 322f
- EXPAR, 323

## F

- FastDigest buffer, 57
  - Fd phage, 20
  - Fe<sup>2+</sup>, 188
  - Fermentas, 56–57, 57f, 128
  - Fidelity
    - methyltransferases, 71–72
    - Type II restriction enzymes, 71–72
  - Fiers, Walter, 50
  - Flavobacterium okeanokoites*, 151
  - FokI, 88, 89, 129, 130t, 147, 149
    - chimeric restriction enzymes, 151–152
    - cloning, 151
    - engineering to obtain hybrid restriction enzymes, 90
    - fusions proteins, 208–209, 306
    - recent studies, 297t
    - recognition sequence, 206, 297t
    - restriction folds, 146f
    - serial analysis of gene expression (SAGE) and, 321
    - structure, 127, 129
    - subunit/domain composition and cleavage mechanism, 206–207
  - FspEI, 323
  - Fusions proteins, 208–209, 210f, 306
- ## G
- Gel-shift assays, 91–92, 92f, 94, 133
  - GenBank, 58
  - Gene targeting tools, 208–211, 210f
    - fusions, 208–209, 210f
    - nickases (nicking enzymes), 209, 211
  - Generalized transduction, 5
  - Genes
    - cloning of genes encoding restriction enzymes, 54–57
      - first R-M systems, 54
      - at New England Biolabs, 54–56
      - in Vilnius, Lithuania, 56–57, 57f
    - codon usage in R-M systems, 125
    - isolation of, 45
    - methyltransferase gene locations adjacent to restriction genes, 3
  - Genetic engineering, 41, 44–46, 305
  - Genetic selection operating at population level, 112
  - Genome editing, 252, 306, 325
  - ghm5C, 241, 246
  - Gibson, Daniel G., 320
  - Gibson Assembly, 318, 320–321, 322f
  - GIY-YIG motif, 191, 306
  - Glover, Stuart, 22, 104, 237
  - gmrD*, 241, 246
  - gmrS*, 241, 246
  - GmrSD, 246
  - Golden Gate Assembly, 318, 319–320, 320f
  - Greene, Patricia, 69
  - Gsul, 130t
  - Gutfreund, Herbert Frederick, 69

## H

- HaeII, 49, 72
- HaeII methyltransferase, 72
- HaeIII, 43, 49
  - mechanisms of base pair recognition, 74–75
  - recognition sequence, 188
  - RNA–DNA hybrids, cleavage of, 72
- HaeIII methyltransferase, 72
- HaeIV, 130t
- Haemophilus influenzae*, 237
  - nontypeable *Haemophilus influenzae* (NTHi), 2, 249, 250f
  - phase variation, 247, 249–252, 250f
- Hairpin adaptor ligation, 322
- Halford, Stephen, 68–70
  - crystal structures of EcoRI and EcoRV, 97
  - retirement party, 198f
- HaloPlex enrichment, 322
- Heitman, Joe, 56, 100
- Helicobacter pylori*, 207, 247–249
- Helix-turn-helix. *See* HTH (helix-turn-helix) motif
- Hershey, Alfred, 19
- Hershey & Chase experiment, 8, 12, 16
- HgaI, 89–90
- HhaI methyltransferase, 128, 153
- HhaII, 244
  - cloning of, 54, 55
  - RNA–DNA hybrids, cleavage of, 72
- Hi-C, 324
- Higa, Akiko, 21
- HincII, 127
- HindfII, 78
- HindI, 75, 251
- HindII, 305
  - recognition sequence, 38–39, 40f
  - recognition sequences in SV40, 39–40
- HindIII, 43
  - 3C and, 324
  - DNA cleavage, 71
  - RNA–DNA hybrids, cleavage of, 72
- HinIII, 77, 110, 111
- HinP11
  - recent studies, 298t
  - recognition sequence, 298t
- History of Restriction Enzymes (October 19–21, 2013) meeting program, 199f, 311–316, 311f
- hm5C, 42, 186, 241, 244, 246
- HNH motifs, 191, 244, 306
- Hoffmann-Berling, Hartmut, 20
- Homing endonucleases, 191, 208, 210f, 325
- Homologous recombination, 307
  - within *hdsS* gene of Type I restriction enzymes, 104–105, 106f
  - stimulated by fusion proteins, 208, 210f
- Horecker, Bernie, 31
- Horizontal transfer, 125, 230, 249, 307
- Host-controlled modification, 21
- Host-controlled variation, 1, 305
  - Bertani and, 5–8, 10–12, 14
  - discovery of, 5–8, 10, 14

- general scheme of adaptive host-induced modification, Luria's, 9t
  - Jean Weigle and, 5–8, 10–12, 14
  - Salvador Luria and, 8, 9t, 11–12
  - HpaI, 43, 49, 74
    - DNA cleavage, 71
    - recognition of ssDNA, 72
  - HpaI methyltransferase, 68
  - HpaII, 43, 49, 67
    - DNA cleavage, 71
    - mechanisms of base pair recognition, 74–75
    - methylation-sensitive amplification polymorphism (MSAP), 323
  - HpaII methyltransferase, 68
  - HphI
    - recent studies, 299t
    - recognition sequence, 299t
  - Hpy99I
    - HNH motif, 191
    - recognition sequence, 191
  - Hpy188I
    - GIY-YIG motif, 191
    - recent studies, 299t
    - recognition sequence, 191, 299t
  - HrpA, 229
  - hsdM* gene(s), 22, 25, 34, 75, 103–104, 215, 251
  - HsdM protein
    - EcoKI, 153, 154f
    - EcoR124I, 224, 225f–226f
    - M-EcoKI (M2S1) complex, 217, 218f
  - hsdR* gene(s), 22, 25, 75, 103–104, 215
  - HsdR protein
    - ATP dependence of motors, 216
    - DNA translocation, 153, 155–161
    - EcoKI, 153, 154f, 225f, 226–228
    - EcoR124I, 222–224, 222f, 225f–226f
    - phosphorylation of, 229–230
    - Res compared, 157
  - hsdS* gene(s), 22, 25, 75, 215
    - cotranscription with *hsdM* gene, 103
    - evolution of DNA specificity of Type I enzymes
      - by homologous recombination within the *hsdS* gene if Type I restriction enzymes, 104–105, 106f
      - transposition within the *hsdS* gene, 107
      - by unequal crossing-over within the *hsdS* gene, 105, 106f, 107
    - phase variation, 251, 252
    - shuffling in *Mycoplasma*, 215
  - HsdS protein
    - circular permutation of EcoAI, 215
    - EcoKI, 153, 154f
    - EcoR124I, 224, 225f–226f
    - M-EcoKI (M2S1) complex, 217, 218f–219f, 219
    - repeats in, 251
    - similarities and differences between Type I families, 215
  - HTH (helix-turn-helix) motif, 129
  - Hubáček, Josef, 22
  - Human, Mary, 8, 11–12
  - Hungarian trick, 55
  - Huntington's disease, 206
  - Hutchison, Clyde, 49
  - Hybrid restriction enzymes, engineering FokI to obtain, 90
  - Hydroxymethylcytosine (hm5C), 42, 186, 241, 244, 246
- I**
- iGEM (International Genetically Engineered Machines) competition, 319
  - Immune system
    - evasion, 247
    - primitive bacterial, 153, 248
  - In vitro DNA assembly technologies, 318
  - Incl plasmid, 231
  - Indels (insertions/deletions), 321
  - In-fusion, 321
  - Insertions/deletions (indels), 321
  - International Genetically Engineered Machines (iGEM) competition, 319
  - Isoschizomers, 43
    - defined, 67
    - differential strand preference for DNA duplexes, 71
    - differentially sensitive to methylation, 67
    - EMBO Workshop in Ghent (1974), 50, 50f
    - neoschizomers, 67
    - Type II restriction enzymes, 66–67
    - Type IIS restriction enzymes, 89
    - usefulness of, 67
- J**
- Jacob, François, 29
  - Janulaitis, Arvydas, 56, 57f
  - Jeffreys, Alec, 255, 255f, 305
  - Jeltsch, Albert, 128
  - Jen-Jacobson, Linda, 72
  - Jennings, Michael, 247
- K**
- Kellenberger, Edouard, 15, 16f, 35
  - Kellenberger-Gujer, Grete, 17, 18, 35
  - Kelly, Tom, 39, 39f, 311f
  - Kinetic studies on DNA cleavage, 94
  - KlcA, 231, 233, 235
  - Kneale, Geoff, 187, 213
  - Knock-in, 325
  - Knockout, 325
  - Kobayashi, Ichizo, 128, 161, 205, 214, 230
  - kor operon*, 233
  - KpnAI, 104
  - KpnBI, 104
  - KpnI
    - HNH motifs, 191
    - recent studies, 299t
    - recognition sequence, 191, 299t
  - Kpn2I, 194t

Krüger, Detlev, 128, 231  
Kühnlein, Urs, 33

## L

*Lactococcus lactis*, 235

Lambda, 305

Arber and, 15, 17

*dgal*, 17

EcoKI action on, 23–24

efficiency of plating variants on different host strains, 17–19, 18t

gene control, 213

host controlled variation and, 5–8, 17–19

methylation, 20

mutants with variation in number of EcoRI sites, 69–70, 70f

Ral protein, 110, 230, 255, 309

restriction of DNA, 41

transduction by, 12–13

Lar protein, 110, 230

Lateral domain movement within genes, 230

LB medium, 13

Lederberg, Esther, 5, 17, 35

Lederberg, Joshua, 17

Lederberg, Seymour, 30

Lehman, Robert, 69

Lenhof, Ed, 31

Lindahl, Tomas, 69

Linn, Stuart, 19–20, 30, 33, 39, 311f

EcoBI purification, 24–25

models for hyphenated and/or palindromic recognition sites, 22–23

Noreen Murray and, 70

LlaBIII, 235–236

LlaGI, 235–236

LongSAGE, 321

Looping. *See* DNA looping

LoxP-Cre recombination system, 5

LpnPI, 323

Lubys, Arvydas, 57f

Lunnen, Keith, 56

Luria, Salvador

barrier to infection, 8

Bertani and, 13–14

Hamilton Smith and, 39

host controlled variation, 8, 9t, 11–12

Joe Bertani and, 5

*A Slot Machine, a Broken Test Tube*, 11, 15

T\* phages, 8, 21

Lysogeny, 5, 8, 10–12

## M

m6A, 204, 206, 235, 238, 244

Macelis, Dana, 50

Mandel, Morton, 21

Mapping, restriction enzyme use in, 44, 321

Mapping epigenetic modification, 323

Markauskas, Algimantas, 57f

Maternal inheritance of mitochondria, discovery of, 44

MboI, 67

3C-based methods and, 324

methyltransferase, 89

recognition site, 194

m4C, 187, 202

m5C, 42, 186–187, 202, 206, 241–242, 244, 246

*Mcr* restriction system, 8, 15, 42, 56

*mcrA* gene, 186

*McrA* protein, 241

*mcrBC* gene, 186

*McrBC* protein, 129, 131, 241, 244, 245f

*McrB-N*, 243f

recent studies, 302t

recognition sequence, 302t

MDEs (modification-dependent restriction enzymes).

*See* Type IV restriction enzymes

M-EcoKI (M2S1) complex, 217–220, 218f–219f

M-EcoKI-Ocr complex, 220

Meganucleases, 208, 210f

Merozygotes, 22

Meselson, Matthew, 16–17, 311f

e-mails with Noreen Murray, 29–34

purification EcoKI, 23–24

Metal cofactors, 127, 188

BamHI, 135

positioning of, 126

role in Type II restriction enzymes, 150–151

*Methanocaldococcus jannaschii*, 219

Methicillin-resistant *Staphylococcus*

*aurus* (MRSA), 230

Methionine, role in DNA modification, 20–21

Methylase-selection method, 55

Methylation

discovery of, 186

host specificity and, 22

maintenance versus de novo methylation by Type I enzymes, 110, 309

mapping epigenetic modification, 323

methionine role in DNA modification, 20–21

methylome, 18, 308

Ral-independent novo methylation in EcoKI M\* mutants, 110, 309

RNA, 238

sensitivity of isoschizomers to, 67

SMRT sequencing to locate sites of, 58

Type I systems, 76

Type II systems, 71

Type III systems, 78, 111–112, 236

Type IIS systems, 89–90

Methylation-sensitive amplification polymorphism (MSAP), 323

Methylome, 18, 308

*Methylobacillus methylotrophus*, 88

Methyltransferases (MTases)

base flipping, 128

circular permutations, 3, 129

common amino acid sequence motifs, 58, 58f

common architecture of, 91

control of restriction and, 212–213, 215

Dam, 67–68, 72, 251

dimeric, 237–238

EcoKI, 217, 218f, 255–256



- EcoKI and EcoR124I (R2M2S1) complex, 220–228
- EcoRI, 89
- fidelity of, 71–72
- genes, cloning, 55
- identification of, 58–59
- methylome, 18, 308
- modeling DNA recognition complex of EcoKI trimeric complex, 153–155, 154f
- monomeric, 71
- monomers, 68, 89, 91
- phase variation, 248, 250f
- RNA, 238
- Type II systems, 71
- Type IIA restriction enzymes, 194
- Type IIG restriction enzymes, 202–203
- Type IIH restriction enzymes, 204
- Type III systems, 238
- Type IIP restriction enzymes, 204
- Type IIS restriction enzymes, 206–207
- Mg<sup>2+</sup>, 205
- DNA binding by Type II restriction enzymes in absence of, 93
- EcoRV DNA cleavage and, 101
- HNH motif, 191
- restriction enzyme requirement for, 41, 42, 68, 89, 91
- Microbiome, 308
- Mismatch repair, strand-directed DNA, 69
- Mitochondria, discovery of maternal inheritance in, 44
- MluCI, 188
- MmeI, 88, 130t, 188, 228, 229f
- LongSAGE, 321
- recent studies, 299t
- recognition sequence, 196, 202, 299t
- specificity alteration, 203
- subunit/domain composition and cleavage mechanisms, 202–203
- Mn<sup>2+</sup>, 188, 191
- MnII
- recent studies, 299t
- recognition sequence, 299t
- mod* genes, 22, 78, 110–111
- Neisseria gonorrhoeae*, 250–251
- phase variation, 249–252, 250f
- Mod subunits of EcoP15I, 159, 236–238, 239f, 240
- Model, Peter, 56, 100
- Modification-dependent restriction enzymes (MDEs). *See* Type IV restriction enzymes
- Modified cytosine restriction. *See* *mcr* restriction system
- Modified single burst technique, 13
- Modrich, Paul, 68–69
- Molecular cloning, 317–318, 318f
- Molecular motors, 127, 152, 155–160, 157f, 160f, 216, 220, 227–228, 240–241, 253, 307
- Molecular switching, 240
- Molecular weight of restriction enzymes, 68, 91
- Montagnier, Luc, 36
- Morgan, Richard, 88, 203
- Mori, Hirotada, 228
- Morse, Larry, 17
- Mosaicism, 188
- Motors. *See* Molecular motors
- Moxon, Richard, 247
- Mrr (modified DNA rejection and restriction), 56, 244
- MRSA (methicillin-resistant *Staphylococcus aureus*), 230
- Mruk, Iwona, 214
- MspI, 67
- methylation-sensitive amplification polymorphism (MSAP), 323
- RNA–DNA hybrids, cleavage of, 72, 73
- MspJI, 244, 246–247
- mapping cytosine epigenetic markers, 323
- recent studies, 303t
- recognition sequence, 303t
- MunI
- recognition sequence, 144, 188
- structure, 127
- Murray, Kenneth, 70
- Murray, Noreen, 161
- Bertani letter to, 5, 10–13
- EcoKI genes, cloning of, 54
- e-mails with Matt Meselson, 29–34
- lambda phages with variation in EcoRI sites, 69–70
- photograph, 199f
- Ral-independent EcoKI M\* mutants, 110, 309
- Type I restriction enzymes, 75
- MUTATE, 53
- MutH, 145, 146f, 149, 200
- MvaI, 139–140, 200
- Mva269I, 207
- recent studies, 299t
- recognition sequence, 299t
- Mycobacterium*, 246
- Mycoplasma*, 215
- Myers, Phyllis, 69
- N**
- NaeI, 88, 129, 130t
- activation in *trans*, 139
- DNA cleavage, 94
- DNA interaction, 140
- recent studies, 299t
- recognition sequence, 299t
- structure, 140
- subunit/domain composition and cleavage mechanisms, 196, 197f
- “Turbo NaeI,” 139
- “Nanoballs,” DNA, 322
- NarI
- recent studies, 299t
- recognition sequence, 299t
- Nathans, Daniel, 321
- Hind II restriction sites in SV40, 39–40
- Nobel Prize, 1, 6, 35, 40
- photograph, 39f
- restriction of SV40 DNA by endonuclease R, 49

- NEAR, 323  
NEB. *See* New England Biolabs (NEB)  
NEBcutter, 53  
NEBuilder Hi-Fi DNA Assembly, 318, 321, 322f  
*Neisseria*, 237, 247, 250–252  
*Neisseria gonorrhoeae*, 142, 250–252  
Neoschizomers, 67  
NESA, 323  
Neutral drift, 188  
New England Biolabs (NEB), 91, 128  
    catalog, 51f, 53  
    cloning genes encoding restriction enzymes, 54–56  
    founding of, 53  
    meetings (1988–2015), 254f  
Next-generation sequencing, 58  
NgoAV, 251, 252  
NgoAXP, 250  
NgoMIV, 129, 135  
    CCGG family of restriction enzymes,  
    193–194, 194t  
    PD...(D/E)XK motif, 149  
    recognition sequence, 142, 185, 193–194,  
    194t, 200  
    structural localization of active site residues, 145f  
    structure and biochemistry, 127, 141–142,  
    143f, 144  
Ni<sup>2+</sup>, 188, 191  
NicE-seq (nicking enzyme-assisted sequencing),  
    324–325  
Nickases (nicking enzymes), 209, 211, 323–324  
*Nocardia aerocolonigenes*, 139  
Nonhomologous enjoining (NHEJ), 211  
Nontypeable *Haemophilus influenzae* (NTHi), 2  
NotI  
    recent studies, 300t  
    recognition sequence, 188, 300t  
    restriction landmark genome scanning  
    (RLGS), 323  
Nt.CviPII, 324  
Nuc endonuclease, 193  
NucA, 147  
Nucleotide excision repair, 232
- O**
- Ocr, 109, 219–220, 223, 231  
    effectiveness of inhibition of Type I  
    R-M systems, 234–235  
    structure, 232–235, 232f, 234f  
OkraI, 205  
Oligo(dT) tailing, 45  
Open chromatin regions, 324–325  
Ostwald viscometer, 37, 38f
- P**
- P1 phage  
    Bertani and, 17–18, 77  
    host-controlled variation and, 18  
    restriction enzymes, 5, 42  
P2 phage  
    Bertani and, 12–14  
    host range variation, 6–8, 7f  
    restriction and modification, 10–12  
PabI  
    DNA glycosylase, 207  
    recent studies, 300t  
    recognition sequence, 300t  
PacI  
    HNH motif, 191  
    recent studies, 300t  
    recognition sequence, 191, 205, 300t  
    subunit/domain composition and cleavage  
    mechanisms, 205–205  
PaeR7I, 54  
Partial diploids, 22  
*Pasteurella haemolytica*, 251  
Pathogenic bacteria, restriction systems in, 2, 308  
pBR322, 317  
PD fold. *See* PD...(D/E)XK motif  
PDB (Protein Data Base), 188, 189f, 190  
PD...(D/E)XK motif, 145–147, 145f, 147f, 185,  
    190–191, 306  
Pettersson, Ulf, 50f  
PfoI, 194t, 199  
Phage selection, use in cloning restriction  
    enzymes, 54, 55  
Phase variation, 187–188, 247–252, 250f, 308  
    pathogen use, 230  
    Type I systems, 251–252  
    Type II systems, 248–249  
    Type III systems, 249–251  
Phosphorothioates, 100–101, 244  
Phylogenetic trees, 148, 148f  
Piekarowicz, Andrzej, 237, 247  
Pin domain, 240–241  
Pingoud, Alfred, 87–88, 97, 126, 128, 193, 253, 305  
Plasmid vectors, 317–318, 318f  
PLD catalytic domain, 191, 193  
PluTI, 201  
Point-of-care DNA amplification and detection,  
    323–324  
Pollock, Mila, 311f  
Pósfai, Janos, 58  
PpiI, 195  
PpuMI, 130t  
Programmed cell death, 214  
Protein Data Base (PDB), 188, 189f, 190  
*Proteus vulgaris*, 211, 246  
*PrrC*, 230  
pSC101, 317  
PspGI, 144  
    CCGG family of restriction enzymes, 194, 194t  
    PD...(D/E)XK motif, 149  
    recent studies, 300t  
    recognition sequence, 194, 194t, 199, 300t  
PstI, 244  
    cloning of, 55  
    *E. coli* strain overexpressing, 55  
PstII, 55  
Ptashne, Mark, 30  
Purification of restriction enzymes, 49

- PvuII  
cloning of genes encoding, 54  
control of restriction, 211–213, 212f  
fusion proteins, 208–209, 210f  
metal cofactors, 151  
molecular weight, 91, 103  
restriction folds, 146f  
structure, 96–97, 102–103, 102f, 146, 186
- PVUII–DNA complex, structure of,  
102–103, 102f
- PvuRtsII, 246  
recent studies, 302t  
recognition sequence, 302t
- PyrG, 229
- Pyrococcus abyssi*, 207
- Q**
- Q-tip helix motif, 157
- R**
- Radzeviciene, Egle, 57f
- Ral (restriction alleviation) protein of  
lambda, 110, 230, 255, 309
- Raleigh, Elizabeth, 56, 57f
- Rao, D.N., 199f
- Rau, Donald, 149
- Reaction mechanisms  
Type I restriction enzymes, 76–77  
Type III restriction enzymes, 78–79
- REBASE database, 50, 52f, 125–126, 126t,  
215, 305
- REBpredictor, 53
- RecA domains, of EcoP15I, 240–241
- Recognition sequence. *See also specific restriction enzymes*  
Arber and Linn models for hyphenated and/or  
palindromic recognition sites, 22–23  
BamHI determination by 2D electrophoresis, 53,  
53f  
Hind II, 38–39, 40f  
Type III restriction enzymes, 78
- Recombinant DNA, Type II restriction  
enzyme use in, 44–46  
gene isolation, 45  
mapping, 44  
repeat DNA sequences, 45  
sequencing, 44–45
- REMAP, 53
- Repetitive DNA sequences, analysis of, 45
- res* gene, 22, 78, 110–111
- Res protein  
DNA translocation, 155–160  
EcoP15I, 155–156, 237–238, 240  
HsdR compared, 157  
sequence subtypes, 157–158
- Resistance transfer factors (RTFs), 21, 29, 41
- Resolvase, 141f
- Restriction alleviation, 160–162, 161f
- Restriction enzymes  
classification of, 41–43  
growth in number of, 49, 51f, 52, 126  
in mid-1970s, 43–44
- Restriction fragment length polymorphisms  
(RFLPs), 255
- Restriction genes, methyltransferase gene  
locations adjacent to, 3
- Restriction landmark genome scanning  
(RLGS), 323
- Restriction sites, of selected enzymes  
studied in recent years, 294t–303t
- Restriction-modification (R-M) genes  
allelism of, 21–23  
location of, 21–23
- Restriction-modification (R-M) systems.  
*See also* Host-controlled variation  
Arber-Dussoix papers, 19  
cloning, 54–57  
codon usage, 125  
control of restriction, 211–213, 212f  
horizontal transfer, 125  
identification using MTase motifs, 58  
nomenclature, 40  
shuffling protein domains, 149
- Reuter, Monika, 128
- RFLPS (restriction fragment length  
polymorphisms), 255
- Rgl1, 42
- Rgl2, 42
- rglA*, 186
- rglB*, 186
- Rich, Alexander, 69
- Richardson, Charles, 38, 69
- RLGS (restriction landmark genome  
scanning), 323
- R-M systems. *See* Restriction-modification  
(R-M) systems
- RNA methylation, 238
- RNA targeting, 325
- RNA-based innate immunity system, 230
- RNA–DNA hybrids, Type II restriction enzyme  
recognition of, 72–73
- Roberts, Richard, 23, 44, 311f  
classification of Type II restriction enzymes, 129  
crystal structures of EcoRI and EcoRV, 97  
Nobel Prize, 49  
photograph, 50f, 57f  
restriction enzyme list, 50, 51f, 305  
restriction enzymes, 49–53
- Rolling circle amplification, 323
- Rosenberg, John, 68–69, 96, 131–132, 311f
- Roullan-Dussoix, Daisy  
Arber-Dussoix papers, 17–19  
EcoBI purification, 24  
EcoRI purification, 41  
host-controlled variation, 17–19  
malaria, 36  
PhD work, 35  
photograph, 18f  
postdoctoral work, 36  
scientific career, 35–36

- RsrI  
DNA binding, 91, 92  
EcoRI similarity to, 188  
recognition sequence, 188  
stable DNA–protein complexes in  
absence of Mg<sup>2+</sup>, 91
- RsuI methyltransferase, 68
- RTFs (resistance transfer factors), 21, 29, 41
- S**
- S-adenosylmethionine (SAM)  
EcoKI, 153, 255  
methylation of DNA, 20  
requirement in restriction enzyme  
purification, 31, 34  
restriction enzyme requirement for, 24,  
41–42, 43, 90, 104  
Type I restriction enzymes reaction  
mechanisms, 76  
Type III enzymes and, 78, 111–112
- “Safety catch,” 201
- SAGE (serial analysis of gene expression), 321
- Sall, 71, 94
- Salmonella*  
*S. potsdam*, 104  
*S. typhimurium*, 147  
Nuc endonuclease, 193  
Type I restriction enzymes, 75–76  
StyLTI system, 110–111  
Type I enzymes from, 103–105
- Sancar, Aziz, 69
- Sanger, Fred, 52, 69
- Satellite repeats, analysis of, 45
- Sau3AI, 67  
3C-based methods and, 324  
cutting of RNA–DNA hybrids, 73  
DNA interaction, 149
- Saul, 230
- SauUSI, 245–246
- Schell, Josef, 50
- ScoA3McrA, 244
- SDA, 323
- Self versus nonself, 307
- Selfishness, 127–128, 161–162
- Sequence discrimination, mechanisms of, 128
- Sequence homologies within and between  
families of Type I enzymes, 104
- Sequencing  
DNase I–based sequencing methods, 324–325  
NicE-seq (nicking enzyme-assisted sequencing),  
324–325  
restriction enzyme use in, 44–45  
single-molecule (SMRT), 58–59, 187, 216  
whole-genome, 230, 307–308
- SeqWare, 58
- Serial analysis of gene expression (SAGE), 321
- SF1 (superfamily 1) proteins, 159
- SF2 (superfamily 2) proteins, 154f, 156, 216, 232,  
241, 253, 306
- SfiI, 129, 130t  
DNA excision, 149  
recent studies, 300t  
recognition sequence, 201, 300t  
structure and biochemistry, 141–142, 145, 201
- SgrAI, 130t, 139  
CCGG family of restriction enzymes, 194t  
recent studies, 301t  
recognition sequence, 201, 301t  
structure, 201, 201f
- Sgr20I, 90
- Sharp, Phillip, 49
- Shuttle vectors, 2
- Sidorova, Nina, 149
- Šikšnys, Virginijus, 128, 142, 185, 194t
- Single-molecule (SMRT) sequencing, 58–59,  
187, 216
- Single-molecule studies  
FokI, 207  
Type I restriction enzymes, 216–217, 307  
Type IIE restriction enzymes, 196, 198  
Type III restriction enzymes, 240–241
- Single-nucleotide polymorphisms (SNPs), 321
- Single-stranded DNA (ssDNA), Type II restriction  
enzyme recognition of, 72–73
- Slab gel electrophoresis, 52, 66
- Slipped-strand mispairing (SSM), 247
- A Slot Machine, a Broken Test Tube* (Luria),  
11, 15
- Smal  
cleavage site, 67  
control by C proteins, 213
- Smith, Hamilton, 311f  
HhaII cloning, 54  
Hind II discovery, 37–40  
Nobel Prize, 1, 6, 35, 40  
photograph, 39f  
Rich Roberts and, 49
- Smith, John, 20, 33  
SMRT sequencing method, 58–59, 187, 216
- SNPs (single-nucleotide polymorphisms), 321
- Solfobolus solfataricus*, 223, 241
- SOS response, 56, 100
- Southern blot, 45, 75
- Specificity  
altered, 127, 203  
evolution of Type I restriction enzymes,  
104–107, 106f, 307  
by homologous recombination within  
the *hdsS* gene,  
104–105, 106f  
by transposition within the *hdsS* gene, 107  
by unequal crossing-over within the *hdsS* gene,  
105, 106f, 107  
Type II restriction enzymes, 66–67, 87,  
88–89, 95  
Type IIS restriction enzymes, 89  
water role in recognition by Type II restriction  
enzymes, 149
- Spi<sup>-</sup> phenotype, 6
- Split genes in adenovirus, 49
- ssDNA (single-stranded DNA), Type II restriction  
enzyme recognition of, 72–73

- SSM (slipped-strand mispairing), 247
- SsoI  
CCGG family of restriction enzymes, 193–194  
recognition site, 193–194
- SsoII, 144  
PD...(D/E)XK motif, 149  
recent studies, 301t  
recognition sequence, 142, 199, 301t
- Stahl, Franklin, 16
- Staphylococcus aureus*  
MRSA (methicillin-resistant *Staphylococcus aureus*), 230  
SauUSI, 245–246
- Star (\*) activity, 95, 188, 205
- Stent, Gunther, 19, 20, 33
- Sticky ends  
EcoRI, 2, 41  
recombinant DNA applications, 45
- Stillman, Bruce, 311f
- Strain typing, 230
- Strand-directed DNA mismatch repair, 69
- Streptomyces coelicolor* A3, 244
- Strominger, Jack, 49
- Structural evolution of Type IIG enzymes  
from Type I enzyme, 228, 229f
- StsI, 89, 207
- Studier, Bill, 109, 158, 231, 307
- StyBII, 104
- StyD4I, 142
- StyLTI, 110, 244  
*mod* gene, 111  
recognition sequence, 111  
*res* gene, 111
- StyLTIII, 106f
- StyR124I, 104
- StySB1, 105
- StySJ, 106f
- StySJb, 105
- StySP1, 105, 106f
- StySQ, 104–105, 106f
- StySQ1, 105
- SuperSAGE, 321
- SUVH5, 243f
- SV40, 39–40, 321
- Swal  
recent studies, 301t  
recognition sequence, 205, 301t  
subunit/domain composition and cleavage mechanisms, 205–205
- SWI2/SNF2 chromatin remodeling  
translocase, 223
- Synthetic biology, 318
- Szczelkun, Mark, 156
- Szybalski, Waclaw, 6f, 206
- T**
- T3 phage  
antirestriction, 231  
resistance to EcoRII, 138
- T4 phage, as dodger of host restriction, 231, 241
- T7 phage  
antirestriction, 231  
Ocr, 109, 219–220, 223, 232–235, 232f, 234f  
resistance to EcoKI cleavage, 109  
resistance to EcoP15I, 112  
resistance to EcoRII, 138
- T\* phages, 21, 186  
barrier to infection by, 8  
Type IV restriction enzymes, 42
- T4 polynucleotide kinase, 38
- TALE nucleases (TALENs), 209, 210f, 306, 325
- TALE (transcription activator-like effector)  
proteins, 208–209, 210f
- TaqI  
DNA binding, 91, 93  
stable DNA–protein complexes in  
absence of Mg<sup>2+</sup>, 91  
Target site location, scheme for, 93, 93f
- Tet (ten-eleven translocation) proteins, 187
- Tetranucleotide hypothesis, Levene's, 16
- TFO (triple-helix-forming oligonucleotide)-linked  
nucleases, 210f
- ThermoFisher Scientific, 57
- Thomas, René, 10
- Tn5, 107, 324
- Tn916, 233
- Tn7 transposase, 149
- TnsA, 145, 146f
- Tracking, by restriction enzymes, 140, 141f
- Transcription activator-like effector (TALE)  
proteins, 208–209, 210f
- Transcriptional control, 214
- Transcriptional regulation of R genes of Type II  
restriction enzymes by control (C)  
proteins and antisense promoters, 55
- Transduction  
Bertani and, 14  
generalized, 5  
lambda, 12–13
- Translocation, 152–153, 155–160, 157f,  
160f, 190, 199, 216–217, 220, 224, 307  
ATP and, 155–156, 158–159, 227  
EcoKI, 155–156, 157f, 158–159, 216–217, 307  
EcoP15I, 237–238, 253  
EcoR124I, 226f
- Transposition, evolution of Type I enzyme DNA  
specificity by, 107
- Triple-helix-forming oligonucleotide  
(TFO)-linked nucleases, 210f
- TseI  
Huntington's disease and, 206  
recent studies, 301t  
recognition sequence, 301t
- TspGWI  
recent studies, 301t  
recognition sequence, 301t
- TstI  
recent studies, 301t  
recognition sequence, 301t  
2D electrophoresis, 53, 53f
- Type I restriction enzymes, 75–77, 103–110,  
152–162, 305–308

- Type I restriction enzymes (*Continued*)
  - antagonists of, 230–232
  - atomic structure, 217–228
    - EcoKI and EcoR124I (R2M2S1) complex, 220–228, 221f–222f, 225f–226f
    - M-EcoKI (M2S1) complex, 217–220, 218f–219f
  - ATP use, 152, 216
  - cleavage models for, 108–109
  - DNA translocation, 152, 155–156, 158–159, 216–217, 226f
  - ecoprrI* system, 230
  - evolution of DNA specificity, 104–107, 106f, 307
    - by homologous recombination within the *hdsS* gene, 104–105, 106f
    - by transposition within the *hdsS* gene, 107
    - by unequal crossing-over within the *hdsS* gene, 105, 106f, 107
  - families and diversity of, 215–216
  - genes and proteins of, 75–76
  - history
    - 1982–1993, 103–110
    - 1993–2004, 152–162
    - 2004–2016, 215–236
    - 1970s and early 1980s, 75–77
  - identification, 58–59
  - maintenance versus de novo methylation
    - by Type I enzymes, 110
  - molecular motors, 155–160, 157f, 160f
  - phase variation, 251–252
  - reaction mechanisms of, 76–77
  - in REBASE (2004), 126t
  - recognition sequences, 76
  - restriction alleviation, 160–162, 161f
  - roles of, 88, 228–230
  - sequence homologies within and between families, 104
  - SMRT sequencing, 216
  - structural evolution of Type IIG enzymes from Type I enzyme, 228, 229f
  - structural genes and family relationships of, 103–104
  - structures and mechanisms of, 107–110
  - Type II enzymes compared, 43, 307
- Type I single protein (Type ISP), 235–236
- Type IA restriction enzymes, 76, 104, 153
  - methylation, 110
  - methyltransferase switch, 255–256
- Type IB restriction enzymes, 76, 104, 110, 153
- Type IC restriction enzymes, 104, 153
  - HsdS protein variation, 251
  - methylation, 110
- Type ID restriction enzymes, 104, 153
- Type IE restriction enzymes, 104
- Type II restriction enzymes, 66–75, 129–152, 305–308
  - amino acid similarities, 188
  - biochemistry of, 67–68
  - catalytic domains, 190–193
  - chimeric, 151–152
  - control of restriction, 211–215
    - by C proteins, 211–214, 212f
    - transcriptional control, 214
  - crystallography, 95–99
  - determination of cleavage sites for, 90–91
  - dimers, 91, 126
  - discovery of, 1, 2
  - DNA binding, 91–93, 92f, 93f
  - DNA cleavage, 70–71, 93–94
  - DNA recognition functions, 99–101
  - DNA–protein interfaces, 99
  - fidelity of, 71–72
  - gene targeting tools, 208–211, 210f
    - fusions, 208–209, 210f
    - nicksases (nicking enzymes), 209, 211
  - generation of new specificities, 88
  - genes and organization, 91
  - growth in number of, 52, 59, 67, 188
  - history
    - 1982–1993, 88–103
    - 1993–2004, 129–152
    - 2004–2016, 188–215
    - 1970s, 37–46
    - 1970s and early 1980s, 66–75
  - identification using MTase motifs, 58–59
  - isochizomers, 66–67
  - metal cofactors, role of, 150–151
  - PD...(D/E)XK motif, 145–147, 145f, 147f, 306
  - percentage of bacteria carrying, 87
  - phase variation, 248–249
  - readout types, 131
  - in REBASE (2004), 126t
  - recognition of RNA–DNA hybrids, 72–73
  - recognition of ssDNA, 72–73
  - recombinant DNA uses, 44–46
  - selected enzymes studied in recent years, table of, 294t–303t
  - specific versus nonspecific enzyme–DNA interactions, 73–74
  - specificities, 66–67, 87, 88–89, 95, 305
  - structures, 127, 306
  - subtypes, 42–43, 128, 129–131, 130t, 185, 193–207, 305
  - subunit/domain composition and cleavage mechanism, 192f
  - transcriptional regulation of R genes by control (C) proteins and antisense promoters, 55
- Type I restriction enzymes compared, 43, 307
- water role in recognition, 149
- Type IIA restriction enzymes, 130t
  - DNA cleavage, 194
  - methyltransferases, 194
  - subunit/domain composition and cleavage mechanisms, 194–195
- Type IIB restriction enzymes, 43, 129, 130t, 228
  - cloning of, 57
  - DNA cleavage, 195
  - subunit/domain composition and cleavage mechanism, 192f, 195–196
  - Type I enzymes compared, 307

- Type IIC restriction enzymes, 43, 90, 130t
    - DNA cleavage, 196
    - subunit/domain composition and cleavage mechanism, 192f
  - Type IIE restriction enzymes, 90, 129, 130t
    - structure and biochemistry, 138–141
    - subunit/domain composition and cleavage mechanism, 196–200, 197f
  - Type IIF restriction enzymes, 90, 129, 130t, 141–145
  - Type IIG restriction enzymes, 54, 129, 130t, 228
    - methyltransferases, 202–203
    - phase variation, 249
    - structural evolution of Type IIG enzymes from Type I enzyme, 228, 229f
    - subunit/domain composition and cleavage mechanism, 192f, 202–203
    - Type I enzymes compared, 307–308
  - Type IIH restriction enzymes, 90, 130t
    - methyltransferases, 204
    - subunit structure, 204
  - Type III restriction enzymes, 202, 235
  - Type IIM restriction enzymes, 129, 130t, 204
  - Type IIP restriction enzymes, 43, 89, 129, 130t
    - cloning of, 57
    - methyltransferases, 204
    - structure and biochemistry, 131–138
    - subunit/domain composition and cleavage mechanism, 192f, 204–206
  - Type IIS restriction enzymes, 129, 130t, 247
    - cloning of, 57
    - Golden Gate Assembly method, 319–320, 320f
    - isoschizomers, 89
    - methyltransferases, 206–207
    - serial analysis of gene expression (SAGE) and, 321
    - specificities, 89
    - subunit/domain composition and cleavage mechanism, 192f, 206–207
  - Type IIT restriction enzymes, 129, 130t, 192f, 207
  - Type III restriction enzymes, 77–79, 110–112, 152–162, 305–308
    - ATP and, 111, 236, 238, 240–241, 253, 307
    - characteristics of, 42
    - DNA cleavage, 111–112
    - DNA recognition and cleavage sequences of, 78
    - enzyme mechanisms, 111–112
    - genetics of, 78
    - history
      - 1982–1993, 110–112
      - 1993–2004, 155–160
      - 2004–2016, 236–241
      - 1970s and early 1980s, 77–79
    - identification, 58–59
    - molecular motors, 155–160, 157f, 160f
    - occurrence and genetics, 110–111
    - phase variation, 249–251
    - reaction mechanisms of, 78–79
    - in REBASE (2004), 126t
    - subclasses, 42–43
      - Type II enzymes compared, 43
      - Type IIS enzymes compared, 89
  - Type IV restriction enzymes, 305, 308
    - discovery of, 42, 186, 308
    - diversity of, 308
    - history (2004–2016), 241–247
    - modification dependence, 186, 241–247
    - in REBASE (2004), 126t
    - Type II enzymes compared, 43
- ## U
- UbaLAI
    - CCGG family of restriction enzymes, 194t
    - subunit/domain composition and cleavage mechanisms, 196, 197f
  - UHRF1, 243f
  - Uracil DNA glycosylase, 319
  - USER (Uracil-Specific Excision Reagent) Enzyme, 318, 319
- ## V
- Van Montagu, Marc, 50
  - Varmus, Harold E., 36
  - Venetianer, Pál, 55
  - Vibrio*, 220
  - Viscometric assay for restriction enzymes, 37, 38f
  - von Hippel, Peter, 72, 87
  - Vsr endonuclease, 145, 146f
- ## W
- Wada, Chieko, 228
  - Walker A and B boxes, 156
  - Watanabe, Tsutomu
    - drug resistance, 21, 29, 41
    - scientific career, 28–29
  - Water, role in recognition by restriction enzymes, 149
  - Watson, James, 5, 52–53
  - Weigle, Jean
    - Edouard Kellenberger and, 35
    - host controlled variation, 5–8, 10–12, 14
    - photograph, 16f
  - Weiserova, Marie, 229
  - Weiss, Bernard, 38, 39f
  - Whole-genome sequencing, 230, 307–308
  - Wilcox, Kent, 37
  - Wilson, Geoffrey, 54–56, 91, 203
  - Winkler, Fritz, 132–134
  - Witkin, Evelyn, 5
  - Wood, William, 19, 30, 31, 33–34
- ## X
- Xeroderma pigmentosum, 232, 308
  - Xmal, 67

**Y**

Yoshimori, Robert, 21, 36, 41  
Yuan, Robert, 31  
  EcoKI purification, 23–24  
  Thomas Bickle and, 42  
  Type I restriction enzymes, 75

**Z**

Zabeau, Marc, 69  
Zavil'gel'skii, G.B., 231, 235  
Zinc fingers, 127, 152, 208, 306  
Zinc-finger nucleases, 208, 210f, 325  
Zn<sup>2+</sup>, 188, 191