

Index

- Abalone*, transgenic for, 247
abl gene, mice transgenic for, 149
Ac element, of *Zea mays*, 44
 β -actin
 gene for, 89
 as promoter, 68, 70, 76, 114, 127
 activist groups, opposition to transgenic animals, 16
 adenine phosphoribosyltransferase, use in Lesch–Nyhan syndrome studies in mice, 153–4
 adenocarcinoma, transgenic mice use in studies of, 152
 adenosine deaminase
 deficiency of, 13
 expression in transgenic rodents, 192
Adh gene, as selectable marker for *Drosophila*, 30
 adrenoleukodystrophy, embryonic stem cell gene targeting studies of, 157
Aedes aegypti, 37
 London strain, cell line from, 48
 meiotic drive in, 55
 target genes for manipulation in, 52–3
 transgenic, 39, 42, 43, 44, 45, 46, 47, 50–1
Aedes albopictus, genomic DNA of, 38
Aedes triseriatus, genomic DNA of, 38
 African catfish, *see Clarias gariepinus*
 Alzheimer's disease, transgenic mice use in studies of, 152–3
Ambystoma, early gene-transfer experiments on, 1
 amphibians, transgenic, 10–11, 245, 250–1
 amyloid precursor protein, role in Alzheimer's disease pathology, 152–3
 androgenetic development, induction in transgenic animals, 10–11
 animal breeding, transgenic animal use for, 3–4, 15, 229–32
 animal genomes, 15
 animals, transgenic, *see* transgenic animals; *see also individual species*
Anopheles spp., transgenic, 245
Anopheles gambiae
 genomic DNA of, 38
 susceptibility of malaria parasite in, 53
 transgenic, 39, 41, 43, 44, 46, 47, 50–51
 trypsin genes from, 57
 X chromosome linkage map of, 53
Anopheles quadrimaculatus, genomic DNA of, 38
Antherea pernyi, genomic DNA of, 38
Anthonomus grandis, transgenic cell culture of, 50–1
 anticancer agents, transgenic animal use in studies of, 150
 antifreeze genes
 expression in transgenic fish, 70, 76, 86
 in gene constructs, 92
 isolation from fish, 87
 α_1 -antitrypsin deficiency, possible gene therapy of, 13, 14–15
Apis mellifera, transgenic, 36, 41, 52
Aplysia californica, transgenic, 248
APOB gene, as cause of familial hypobetalipoproteinemia, 154
apo genes, in atherogenesis studies, 154–5
 apolipoprotein lipoprotein genes, 89
 aquaculture, transgenic fish use in, 84–6
 arachnids, transgenic, 248–9
 arginosuccinic aciduria, gene therapy of, 13
Artemia, transgenic, 248
 arthritis, transgenic mice use in studies of, 153

- Aspergillus* spp., transgenic, 245
 atherosclerosis, embryonic stem cell gene targeting studies of, 154
 Atlantic salmon, *see Salmo salar*
 avian leukosis virus, in transgenic bird preparation, 117
 axolotl, *see Ambystoma*
- bacteria, transgenic, 245
 bacterial plasmids, as gene-vector systems, 2
 bacterial viruses, as gene-vector systems, 2
 bacteriophage P1, in site-specific genome recombination system, 166–7
 bacteriophages, transgene integration effected by, 8
 badgers, as rabies vectors, 16
 BAG vector, in retroviral vector system, 194
 behavior, possible modification by gene therapy, 14
- bGH* gene
 birds transgenic for, 117–18
 cattle transgenic for, 117–18
 binary system, for regulating mouse gene expression, 166
 biolistics technique, for gene transfer in insects, 40–1
 birds; *see also* poultry
 chimeras of, 119–21, 126–9
 eggs of in genetic engineering, 106
 embryology of, 109–14
 karyotypes of, 107
 reproduction of, 107–14
 spermatozoa of, 107–8
 transgenic, 106–37
 black-fly, *see Simulium vittatum*
 blastoderm
 manipulation *in situ* in birds, 125–6
 in transgenic bird preparation, 115–19, 129
 blood coagulating factor IX, secretion by transgenic sheep, 217
 Bloom's syndrome, embryonic stem cell gene targeting studies of, 157
- Bombyx mori*
 genomic DNA of, 38
 transgenic, 15, 23, 36, 40, 50–1, 52, 245
 botulinus toxin, 17
 bovine growth hormone gene, in gene constructs, 92
- Brachydanio rerio*
 gene isolation from, 88, 89
 transfection of embryonic stem cells of, 11
- transgenic, 9, 63–4, 65, 67, 70, 72, 83, 85, 89, 90, 91
 brine shrimp, *see Artemia*
 Busulphan, 128
- Caenorhabditis elegans*
 mutagenic studies of embryonic development in, 161
 transgenic, 245, 246–7
 calcium phosphate precipitation method, 48
 cancer, transgenic mice use in studies of, 149–51
- Carassius auratus*
 gene isolation from, 89
 transgenic, 63, 64, 89, 91, 92, 94
 carbamoylphosphate synthetase deficiency, possible gene therapy of, 13
 carcinogens, transgenic animal use in studies of, 150
 Carnegie vectors, preparation of, 29–30
 carp, *see Cyprinus carpio*
 catfish, *see Clarias gariepinus; Ictalurus punctatus*
 CAT gene, 6, 48
 in gene constructs, 89, 90, 114, 194, 226, 249, 250
 as reporter gene, 6, 9, 68, 71, 72, 76, 85
Catostomus commersoni, gene isolation from, 88
- cattle
 cell lines from embryos of, 189, 191
 transgenic, 221–9, 245
 gene-transfer efficiency in, 183
 zygote production for, 222–6
 cell ablation studies, on transgenic *Drosophila*, 35–6
 cell cultures, transgene copy transfection of, 11
 cell lines
 from large mammals, 189–90
 transgene introduction into, 48–9
 from transgenic fish, 70
Ceratitis capitata, transgenic, 40, 43, 50–1
- c-fos* gene
 function studies on, 148–9
 in osteopetrosis studies, 156
 channel catfish, *see Ictalurus punctatus*
 chaoptic promoter, in *Drosophila* cell ablation studies, 36
 cherry salmon, gene isolation from, 89
 chicken lysozyme gene, 9
 chickens
 chimeras of, 119–21
 sperm-mediated gene transfer in, 41
 transgenic, 106–37, 192, 245

- chimeras
 of birds, 119–21
 of mice, 142–43
- China, genetic engineering views of, 16
- Chinese carp, gene isolation from, 88
- chinook salmon
 gene isolation from, 88
 growth hormone in gene constructs, 94
 transgenic, 76
- Chironomus tentans*, genomic DNA of, 38
- chloramphenicol acetyltransferase gene,
see CAT gene
- chromosome-mediated gene transfer, in
 fish, 66–7
- chum salmon, gene isolation from, 87, 88,
 89
- ciliary neurotropic factor, in stem cell cul-
 tures of farm animals, 189
- citrullinemia, gene therapy of, 13
- Clarias gariepinus*, transgenic, 63, 90
- coagulation-factor deficiencies, gene ther-
 apy of, 13
- coding sequences, 15
- coho salmon
 gene isolation from, 88, 89
 growth hormone gene of, in gene con-
 structs, 94
- complement-factor deficiencies, gene
 therapy of, 13
- concatamerization of DNA
 in transgenic fish, 78, 82
 in transgenic mice, 141
- corticotropin releasing factor precursor
 gene, 88
- cosmids, as gene-vector systems, 186
- cotton boll weevil, *see* *Anthonomus
 grandis*
- Crassostrea*, transgenic, 247–8
- Cre recombinase
 in gene integration, 8
 in site-specific genome recombination
 system, 166–7, 169
- Crithidia* spp., transgenic, 246
- crucian carp, transgenic, 92
- crystallin gene, expression in transgenic
 fish, 68, 70
- β -crystallin gene, 88
- γ -crystallin gene, 88
- δ -crystallin gene, 91
- c-ski* gene, pigs transgenic for, 206
- c-src* gene, in osteopetrosis studies, 156
- ctfr* gene, as cause of cystic fibrosis, 155–
 6
- Culex* spp., rickettsia-like microorganisms
 in, 42
- Culex pipiens*, genomic DNA of, 38
- cuticle pigmentation, as selectable marker
 for *Drosophila*, 30
- Cyprinus carpio*
 gene isolation from, 87, 88, 89
 transgenic, 18, 63, 76, 83, 90, 93
- cys E* gene, sheep transgenic for, 213
- cys K/cys M* gene, sheep transgenic for,
 213
- cystic fibrosis
 embryonic stem cell gene targeting
 studies of, 155
 possible gene therapy of, 12, 13
- cytoplasmic injection technique, 6
- cytoskeletal actin gene, sea urchins
 transgenic for, 250
- Dejerine–Sottas neuropathy, embryonic
 stem cell targeting studies of, 156
- dextran sulphate method, 48
- diabetes mellitus
 possible gene therapy of, 14
 transgenic mice use in studies of, 151
- differentiating inhibitory activity, 142
- dihydrofolate reductase, expression in
 transgenic rodents, 192
- diphtheria toxin, in cell ablation studies,
 84, 169
- diseases
 gene therapy for, 2, 12–13
 human, transgenic animal use in studies
 of, 151–7, 180
 insect-borne, transgenic insect use for
 control of, 52–4
 resistance to, in transgenic farm ani-
 mals, 206–209
- DNA
 degradation in alimentary canal, 17
 isogenic, in gene targeting, 148
 wild-type, soaking mutant insect em-
 bryos in, 22
- DNA methylation
 gene inactivity related to, 74
 transgenic animal use to study, 3
- dogs, avian retrovirus in cell line from,
 193
- dot/slot blotting method, 80
- double induction process, 11–12
- Drosophila hydei*, *mariner* element of, 24
- Drosophila mauritiana*, *mariner* element
 of, 24
- Drosophila melanogaster*
 GAL4 expression in, 166
 genomic DNA of, 38
 homeotic genes of, 164
 mutagenic studies of embryonic devel-
 opment in, 161

Drosophila melanogaster (cont.)

- transgenic, 248–9
 - cell ablation studies on, 35–6
 - embryo collection and preparation, 25–7
 - enhancer trapping in, 35
 - experimental design and analysis, 32–3
 - germ-line transformation, 24–5
 - historical aspects, 21–4
 - host strain characteristics, 25, 27–8
 - insertional mutagenesis of, 36–7
 - microinjection, 27–8
 - transformation vector constructs, 28–32
 - use in *Drosophila* genetics, 33–6
 - use of, 48
- drugs, *see* pharmaceuticals
- DT-A* gene, 147
- ducks, chimeras of, 121
- dynein heavy chain gene, 88
- egg cytoplasm, transgene introduction into, 8
- eggs
 - DNA introduction into, 5, 6–7
 - of poultry, in genetic engineering, 106
 - in transgenic bird preparation, 108–9
 - in transgenic mouse formation, 138
- electroporation
 - of fertilized egg, transgene introduction by, 65–6
 - of sperm, DNA introduction by, 5, 6–7
 - transgene introduction by, 48, 246
- elliptocytoses, gene therapy of, 13
- embryo chimeras, of birds, 126–9
- embryo culture, in transgenic bird preparation, 114–15
- embryonic stem cells (ES cells)
 - gene disruption in, 169
 - gene transfer in large mammals by, 180, 188–91
 - gene trapping in, 161–3
 - insertional mutagenesis in, 161
 - transgene copy transfection of, 11
 - transgene induction in, 5
 - in birds, 109, 119–20, 129
 - in fish, 67, 83
 - marker genes for, 147
 - in mice, 138, 142–4, 147
- embryos, of large mammals, 189–90
- emphysema, α_1 -antitrypsin deficiency in, 14
- enhancer elements, 10
 - transgenic animal studies on, 6
- enhancer sequences, transgenic animal use to study, 3

- enhancer trap strategy, in mouse gene trapping studies, 161–2
- env* gene, of retroviruses, 116, 192
- Ephesia kuhniella*, transgenic, 23
- epidermal growth factor, in stem cell cultures of farm animals, 189
- e*-genes, silencer elements in, 10
- Escherichia coli*, DNA organization of, 37
- Esox lucius*
 - gene isolation from, 88
 - transgenic, 63, 76, 92
- evolution, 15
- Fabry disease, possible gene therapy of, 13
- farm animals, transgenic, 179–244; *see also individual animals*
 - breeding of, 229–32
 - disease resistance in, 206–9
 - gene constructs for, 183–4
 - program for production of, 183, 185
- fertilized egg
 - electroporation, 64–5
 - injection of, 64–5
- F1 generation, in transgenic animals, 11
- fibroblast growth factor, in stem cell cultures of farm animals, 189
- filarial worms, mosquito susceptibility to, 52–3
- fish, transgenic, 63–105, 245
 - in aquaculture, 84–6
 - concatamerization of DNA in, 78
 - copy number injected, 73–5
 - DNA degradation in, 79
 - DNA integration into, 78–9, 80–3
 - DNA replication in, 78
 - ethical considerations, 86–7
 - fate of injected DNA in, 77–8
 - form of injected DNA in, 80
 - gene ablation and function reduction in, 83–4
 - gene constructs used for, 89
 - integration mechanics in, 70–1
 - linear or supercoiled DNA in, 79–80
 - methodology for, 5
 - mosaicism in, 10, 78–9, 81, 83
 - promoter choice, 67–8, 70
 - prospects for, 84–7
 - release of, 18
 - reporter gene use in, 71–3
 - in studies of gene regulation and fish physiology, 84–7
 - transgene construct design and expression in, 67–70
 - transgene expression in, 75, 76
 - transgene introduction methods, 64–7

- transgene markers in, 70–1, 76
- transgene transmission by, 83
- flounder, gene isolation from, 87
- FLP/FRT recombinase system, in non-drosophilids, 45–6
- FLP recombinase, in site-specific genome recombination system, 166–7
- FL recombinase system, catalysis of site-specific recombination by, 8
- food, transgenic animals as, 15
 - safety issues, 15, 17
- foxes, as rabies vectors, 16
- fragile X syndrome, embryonic stem cell gene targeting studies of, 157
- frogs, transgenic, 23
- fruit fly, *see Drosophila melanogaster*
- fucosidosis, possible gene therapy of, 13
- fungi, transgenic, 245
- furunculosis, in salmon, 86

- G418, as selective agent, 9, 31, 42, 77
- gag* gene, of retroviruses, 116, 192
- β -galactosidase, expression in transgenic birds, 120
- β -galactosidase gene, 9
 - in gene constructs, 91, 114
- β -gal* gene, 9
- Gal4* gene, in transgenic mouse binary system, 166
- gancyclovir, as selective agent, 31, 42, 77, 147
- Gaucher's disease
 - embryonic stem cell gene targeting studies of, 154
 - gene therapy of, 13
- gender imprinting
 - transgenic animal use to study, 3
 - in transgenic mammals, 10
- gene ablation, 11
- gene farming, in large mammals, 181, 215–17
- gene guns, transgene introduction in fish by, 66
- gene promoters, transgenic animal use to study, 3, 5
- gene targeting, 11–12
 - of embryonic stem cells, 5
 - in rodents, 144–8
 - in studies of human genetic disorders, 153–6
- gene therapy
 - for inherited disease in humans, 2, 12–14
 - possible misuse of, 14
 - possible proto-oncogene activation in, 14
 - U.S. and U.K. authorization for, 12
- genetic aberrations, germ line specific, 22
- genetic defects, transgenic animal use in studies of, 151
- genetic disorders, use in genetic disease studies, 153–6
- gene trapping, in mouse embryonic stem cells, 161–3
- genomic imprinting, in transgenic mice, 158–9
- Germany, genetic engineering authorization in, 16
- germ-line transformation, in transgenic animals, 5
 - in *Drosophila*, 24–5
- gilthead sea-bream, gene isolation from, 88
- α -globin, as promoter, 140
- α -globin gene
 - in gene constructs, 92, 210
 - isolation from fish, 89
 - in transgenic mice, 151
- β -globin gene
 - in gene constructs, 210
 - in transgenic mice, 151, 192
- glucocerebrosidase gene, role in Gaucher's disease, 154
- glucose-phosphate isomerase, as transgenic marker, 143
- goats, transgenic, 217–220
 - breeding of, 230
 - gene-transfer efficiency in, 183
- gold, in gene guns, 5, 66
- goldfish, *see Carassius auratus*
- gonadotropin gene, 89
- gonadotropin α -gene, 89
- gonadotropin β -gene, 89
- gpt* gene, 147
- granulocyte actin deficiency, gene therapy of, 13
- grass carp, gene isolation from, 87, 89
- Green Party, opposition to transgenic animals, 16
- Greenpeace, opposition to transgenic animals, 16
- growth hormone
 - animals transgenic for, 17
 - pigs, 204–5
 - sheep, 213
 - of fish, gene cloning for, 86, 87, 88
 - as promoter, 70
- gynogenetic development, induction in transgenic animals, 10–11
- gypsy* element, as transformation vector, 44

- haemoglobin, synthesis in transgenic pigs, 209–10

- haemoglobinopathies
 - gene therapy of, 13
 - transgenic mice use in studies of, 151
- hamster, cell lines from embryos of, 189
- health issues, posed by transgenic animals, 15–19
- heat shock promoter
 - gene isolation for, 89
 - in gene transfer method
 - for birds, 120
 - for insects, 40, 46, 48
 - induction in *Drosophila* embryo, 31
- helper element, for transposase, 29, 31
- hereditary angioneurotic or edema, gene therapy of, 13
- heterozygote fitness, 55
- H19* gene, imprinting of, 156
- high-density lipoprotein cholesterol levels, transgenic mice use in studies of, 153, 154
- high-mobility group protein gene, 88
- histone gene, 87
- hobo* element, as transformation vector, 31
 - in *Drosophila*, 24
 - in mosquitoes, 44
- homeobox-containing gene, 88
- honeybee, *see Apis mellifera*
- 'hot spots', as preferential gene sites, 32
- housefly, *see Musca domestica*
- Hox* gene, mutation induction of, 164–5
- hPc* gene, pigs transgenic for, 209
- hPc* gene, targeting of, 144–5, 147
 - use in genetic disease studies, 153–4
- hspneo* DNA, in transgenic mosquito cell line, 49
- human diseases and disorders, transgenic animal use in studies of, 151–7, 180
- human factor IX, in transgenic sheep
 - gene constructs, 14
- human growth hormone gene
 - in gene constructs, 68, 92–93
 - metallothionein I spliced to, 68
- human interleukin for DA cells, 142
- Huntington's disease, embryonic stem cell gene targeting studies of, 157
- hybrid dysgenesis, 22
- 4-hydroxy-3-nitrophenylate, mouse monoclonal antibody against, 207
- hygromycin gene
 - in gene constructs, 91
 - as marker gene, 147
- hygromycin phosphotransferase gene, integration of, 8
- hypophosphatasia, possible gene therapy of, 13
- Ictalurus punctatus*
 - gene isolation from, 88
 - transgenic, 63, 91, 92, 93, 94
- I* element, in *Drosophila*, 24
- Igf2* gene, imprinting of, 156, 157
- immunoglobulin
 - as enhancer/promoter, 68
 - gene constructs for, 206–8
 - heavy chain gene of, 88
- Indian major carp, transgenic, 93
- inflammatory disease, transgenic mice use in studies of, 153, 156
- influenza virus, gene-therapy protection for, 12, 206, 207
- insects
 - non-drosophilid
 - FLP/FRT recombinase system in, 45–6
 - genome organization of, 36–7
 - mobile genetic elements in, 44–5
 - phenotypic markers for, 46
 - stage- and tissue-specific promoters for, 47
 - transgenic, 21–62
 - biolistics method for, 40–1
 - DNA vector systems for, 42–4
 - Drosophila melanogaster*, 21–36
 - economic aspects of, 49, 53–4
 - embryo microinjection method for, 38–40
 - mosquitoes, 38–40
 - in natural populations, 54–5
 - potential application of, 48–55
 - release of, 18, 55–6
 - sperm-mediated transformation method, 41
 - symbiont transformation method, 42
 - target genes for manipulation in, 52–4
 - insertional mutagenesis
 - in *Drosophila*, 22
 - in mice, 159–60
 - insulin, use in stem cell cultures of farm animals, 189
 - insulin gene, 89
 - insulin-like growth factor gene, 89
 - integrases, as site-specific recombinases, 8
 - int-2* gene, in transgenic mouse binary system, 166
 - introns, effect on gene expression, 10
 - inverted terminal repeats (ITRs), in transgenic *Drosophila* formation, 28, 29, 31
 - isotocin gene, 88
 - isotocin precursor gene, 88

Index

261

- ITR binding protein, role in transgenic *Drosophila* formation, 28
- Jumpstarter* element, transposase generation by, 34
- Kennedy disease, embryonic stem cell gene targeting studies of, 157
- lac* gene, as reporter gene, 6, 68, 71, 72, 85, 114, 115, 120, 161–3, 168, 169
- lactoferrin gene, expression in transgenic cattle, 229
- β -lactoglobulin
 expression in transgenic sheep, 216–17
 promoter for, in gene constructs, 14
- lac Z* gene, from *E. coli*, 35
- lambda-phages, as gene vector systems, 186
- large transgenic mammals, 179–244
- legislation, affecting transgenic animals, 3, 15–19, 68
- Leishmania* spp., transgenic, 246
- Lesch–Nyhan disease
 embryonic stem cell gene targeting studies of, 153–4
 possible gene therapy of, 13
- leukaemia inhibitory factor
 in cell lines, 142
 use in stem cell cultures of farm animals, 189
- leukaemic cells, transfection of cultures of, 11
- limb-deformity phenotype, in transgenic mice, 160
- Lipofectin, in intragenic bird preparation, 120, 123, 127
- lipofection method, transgene introduction by, 5, 6–7
 into cell lines, 48
 into fish, 67
- liver cancer, transgenic mice use in studies of, 151–2
- loach, *see Misgurnus fossilis*
- locus control regions, in transgenic animals, 141, 184, 210
- locust, *see Locusta migratoria*
- Locusta migratoria*, 50
- long-period interspersion (LPI), in DNA organization, 37
- loxP*-flanked β -galactosidase reporter gene, integration of, 8
- loxP* sequence, in site-specific genome recombination, 167–8
- LUC* gene
 in fish transgene construct, 65, 76
 integration of, 8
 as reporter gene, 6, 9, 41, 85, 91, 125
- Lucilia cuprina*
 genomic DNA of, 38
 transgenic, 41, 43, 46, 50–1
- Lytechinus variegatus*, transgenic, 249–50
- malaria
Anopheles gambiae as major vector for, 38
 parasite for, 53
- male recombination, in *Drosophila*, 21–2
- mammals, large transgenic, 179–244
- mammary gland
 of transgenic cattle, 229
 of transgenic goats, 220
 of transgenic pigs, 209
 of transgenic sheep, 216
- mariner* element
 generation of hybrid dysgenic phenomena, in *Drosophila*, 24
 as transformation vector in *Drosophila*, 24
 as transformation vector in mosquitoes, 44
- Masu salmon, gene isolation from, 88
- matrix-attachment regions (MARs), regulation of gene expression by, 9
- meal moth, *see Ephesia kuhniella*
- medaka, *see Oryzias latipes*
- medfly, *see Ceratitis capitata*
- meiotic drive, in insects, 54–5
- melanin-concentrating hormone genes, 89
- metachromatic leukodystrophy, possible gene therapy of, 13
- metallothionein
 gene isolation from fish, 87
 as promoter, 68, 70, 120, 148, 165, 204
- Metaseiulus occidentalis*, transgenic, 245, 248–9
- MHC antigen gene, 88
- mice
 antibody genes of, 54, 206–7
 binary system for regulating gene expression in, 166
 chimeras of, 142
 inducible gene expression in, 165–9
 primordial germ cells of, 122–3
 saturation mutagenesis in, 161
 site-specific recombination system use of genome manipulation in, 166–9
 transgenic, 21, 22, 138–78, 192, 245
 applications of, 148–63
 generation of, 138–148
 gene-transfer efficiency in, 183

- mice (*cont.*)
 insertional mutagenesis in, 159–60
 lineage tracing studies on, 169
 methodology for, 4–5
 prospects for, 163–5
- microinjection technique
 in birds, 106–7, 114–15
 in cattle, 223, 226
 in *Drosophila*, 24
 embryo transfer by, 27–8, 39–41
 in large mammals, 179–80, 182–8, 201
 in sheep, 212
- minos* element, as transformation vector
 for *Drosophila*, 24
- mirror carp, transgenic, 93
- Misgurnus fossilis*, transgenic, 63, 64, 91, 92
- MTV–human TFG α fusion gene, in
 adenocarcinoma studies, 152
- molluscs, transgenic, 18, 247–248
- Moloney murine leukaemia virus, use in
 transgenic mouse formation, 140
- monophosphotransferase, *Drosophila*
 gene coding for, 31
- mosaicism, in transgenic animals, 2, 5, 10
- Mos20 fibroblast cell line, transgene intro-
 duction into, 48, 49
- mos* gene, function studies on, 149
- mosquitoes; *see also* *genus/species*
names
 genomic DNA of, 38
 transgenic, 42, 44, 46
- mouse mammary tumor virus, 149
- Mov-13* gene, as cause of embryonic le-
 thal mutant, 160
- M strain polytene chromosomes, of *Dro-*
sophila, 34
- MT-1-rGH* fusion genes, effect on
 transgenic mouse body weight,
 166
- Musca domestica*
 genomic DNA of, 38
 transgenic, 50–1
- mussels, *see* *Mytilus edulis*
- mutagenesis, in mice, 159–60
- mutations, transgenic animal use to
 study, 3
- Mxl* gene, pigs transgenic for, 206, 207,
 208
- myc* gene, mice transgenic for, 149–50
- myosin, as promoter, 70
- myosin gene, 87
- myotonic dystrophy, embryonic stem cell
 gene targeting studies of, 157
- Mytilus edulis*, transgenic, 247
- nematodes, transgenic, 23, 245, 246–7
- neo* gene
 expression of, 31, 163, 192
 in gene constructs, 91, 246, 249
 as reporter gene, 9, 71, 147
- neomycin, *neo* gene system resistance
 to, 9
- Netropis lutrensis*, gene isolation from,
 88
- neurofibromatosis, embryonic stem cell
 gene targeting studies of, 157
- nodal* gene, characterization of, 161
- Northern blot analysis, of *Mxl* transgenic
 pigs, 208
- northern pike, *see* *Esox lucius*
- nucleic acid hybridization, in gene recog-
 nition and transfer, 2
- oilseed rape, transgenic, 18
- oncogenes, expression in transgenic
 mice, 149
- OncoMouse, 149
- Oncorhynchus mykiss*
 gene isolation from, 87, 88, 89
 transgenic, 63, 65, 68, 74, 82, 83
- oocytes, DNA introduction into, 5, 64
- opsin gene, 89
- Oreochromis niloticus*
 gene isolation from, 87
 transgenic, 63, 65, 68, 90, 92
- ornithine transcarbamylase deficiency,
 possible gene therapy of, 13
- Oryzias latipes*, transgenic, 63–4, 68, 83,
 89, 91, 92, 93
- oskar* gene, of *Drosophila* primordial
 germ-cells, 126
- ovalbumin* gene, in transgenic birds, 127
- oysters, *see* *Crassostrea*
- pancreatic acinar tumors, from *ras* onco-
 gene, 150
- Paramecium* spp., transgenic, 246, 247
- Paramecium tetraurelia*, transgenic, 246
- particle bombardment of egg, for DNA in-
 troduction, 5, 6
- P1 *Crellox* recombination system, 8
- P* element, as transformation vector, 7, 8
 in insects, 55, 248
 requirements, 29
 for transgenic *Drosophila* formation,
 22, 24, 25, 28–9, 30, 33–5
 for transgenic non-drosophilid forma-
 tion, 43–4
- pharmaceuticals, from transgenic ani-
 mals, 2, 14–15, 220

Index

263

- phenotypic markers, for incorporation into non-drosophilid transformation vectors, 46
- phenylketonuria, gene therapy of, 13
- pigs, transgenic, 14, 182, 193, 194, 195–210, 245
- breeding of, 230, 231, 232
 - disease resistance studies, 206–8
 - formation methods, 195–203
 - gene constructs for, 205
 - gene-transfer efficiency in, 183
 - human haemoglobin synthesis in, 209–10
 - transgene expression in mammary gland, 209
- Placopecten*, transgenic, 247
- plaice, gene isolation from, 87
- plants, transgenic, 4, 18, 23, 245
- plasmids, as gene vector systems, 4, 186
- pol* gene, of retroviruses, 116, 192
- polybrene method, transgene introduction into cell lines by, 48
- polymerase chain reaction (PCR)
- transgene integration detection by, 6, 41, 45, 80–1, 195, 228
 - use in insect genome mapping, 38–9
- polyspermy, in birds, 106
- position effects, transgenic animal use to study, 3
- positive–negative selection system, in gene targeting, 145, 146
- poultry, breeding practices for, 106
- pP3PALacZ–Carp β A gene construct, restriction map of, 69
- pP3PALacZ–Rat β A gene construct, restriction map of, 69
- predatory mite, *see Metaseiulus occidentalis*
- pregrowth hormone gene, 87, 88
- premature growth hormone, 87
- preprogonadotropin releasing hormone gene, 89
- preproinsulin gene, 89
- primordial germ-cells (PGCs)
- isolation of, 122–3
 - screening of, 124
 - transfer and proliferation of, 124–5
 - in transgenic bird preparation, 109, 120–2, 129–30
- prolactin gene, 88
- promoter sequences
- choices of, 15
 - combination with structural genes in pharmaceutical production, 14
- pronuclear injection
- insertional mutagenesis by, 160
 - use in transgenic rodent formation, 138, 140–2
- propionyl CoA-carboxylase deficiency, possible gene therapy of, 13
- protamine gene, 88
- proteins, production in transgenic large mammals, 180
- proto-oncogenes, possible activation by gene therapy, 14
- protozoans, transgenic, 245–6
- pseudonucleus, formation around exogenous DNA, 8
- P* transposable element family, 21–2
- p54 tumor-suppressor protein, 156
- pUChsneo vector
- for transgenic *Drosophila* formation, 31, 32
 - for transgenic insect formation, 42
- pUC8 plasmid, in transgenic *Drosophila* formation, 30
- purine nucleoside phosphorylase deficiency, gene therapy of, 13
- quail
- embryology of, 112
 - transgenic, 120
- rabbits
- sperm-mediated gene transfer in, 41
 - transgenic, 182, 194, 228, 229, 245
- rainbow trout, *see Oncorhynchus mykiss*
- ras* gene, mice transgenic for, 149, 150
- rat growth hormone, in gene constructs, 93
- rats, transgenic, 138, 245
- Rb* gene, 147
- red carp, transgenic, 93
- red sea-bream, gene isolation from, 87
- re* gene, mosquitoes transgenic for, 55
- 5' regulatory region, effect on integrated gene expression, 10
- regulatory sequences, transgenic animal use in studies of, 5–6
- Ren* gene, 147
- repetitive DNA family, 88
- replication-defective vectors, for transgenic birds, 118–19
- reporter genes, use in transgenic animal studies, 6, 9
- restriction enzymes, use in gene transfer, 1
- reticuloendotheliosis virus, use in transgenic bird preparation, 108
- retinoblastoma, transgenic mice use in studies of, 151–2
- retroposon-like gene, 88

- retrotransposons
 in fish, 85
 as gene vectors, 24
- retroviruses
 as gene vectors, 5, 8, 13, 24
 in birds, 115–19
 in fish, 70
 in large mammals, 192–4
 in mice, 138, 140
 safety factors for, 193–4
 terminal repeat sequences of, 7
 use in insertional mutagenesis in mice, 160
- ricin toxin, in cell ablation studies, 36, 84
- rickettsia-like microorganisms, in tsetse flies, 42
- RNA polymerase, consensus sequence recognition by, 6
- rodents, transgenic, 138–78
 applications of, 148–63
 in assessment of gene function, 148–9
 in oncogenicity studies, 149–51
 prospects for, 163–5
- rosy*, as selectable marker for *Drosophila*, 30, 31
- rough* gene, as selectable marker for *Drosophila*, 30
- Rous sarcoma virus, promoter from, 9
 use in transgenic cattle, 226, 228
 use in transgenic fish, 68
- Russia, genetic engineering views of, 16
- Saccharomyces cerevisiae*, use in site-specific genome recombination system, 166–7
- salivary gland-specific promoter sequence, in *Aedes aegypti*, 47
- salmon, *see Salmo salar*
- salmonids
 endogenous retrovirus in, 70
 gene isolation from, 87, 88, 89
 transgenic, 63, 65, 76, 83, 90
- Salmo salar*
 gene isolation from, 87, 88, 89
 transgenic, 63, 76, 83, 86, 92, 94
- Sandhoff disease, possible gene therapy of, 13
- Sarcophaga bullata*, genomic DNA of, 38
- satellite DNA, 88
- scallops, *see Placopecten*
- sea bass, *see Sparus auratus*
- sea-bream, transgenic, 91
- sea slug, *see Aplysia californica*
- sea urchins, transgenic, 23, 41, 245, 249–50
- serum albumin gene, 89
- sevenless* enhancer, use in *Drosophila* cell ablation studies, 36
- sheep, transgenic, 182, 193, 245
 formation, 210–17
 gene constructs for growth hormone cascade, 213
 gene-transfer efficiency in, 183
 use in pharmaceutical production, 14, 15
 wool production improvement in, 213–15
- sheep blow-fly, *see Lucilia cuprina*
- 'shiverer' mutant mice, transgenic animal use in studies of, 151
- short-period interspersion (SPI), in DNA organization, 37
- sickle cell disease, transgenic mice use in studies of, 151
- silencer elements, in genes, 10
- silkworms, *see Bombyx mori*
- silver crucian carp, transgenic, 93
- Simulium vittatum*, trypsin gene from, 47
- site-specific recombination systems, use for genome manipulation, 166–9
- slime moulds, transgenic, 23
- somatic gene transfer, in farm animals, 181–2
- Southern blotting method, transgene integration detection by, 6, 25, 80–1, 83, 195
- Sparus auratus*, transgenic, 63
- sperm, in transgenic bird preparation, 107–8
- sperm electroporation, transgene introduction in fish by, 66
- sperm-mediated gene transfer
 in insects, 41
 in large mammals, 194, 195
- spleen necrosis virus, in transgenic bird preparation, 118–19
- Spm* element, of *Zea mays*, 44
- steel factor, in stem cell cultures of farm animals, 189
- stem cells, in gene therapy, 12
- Strongylocentrotus purpuratus*, transgenic, 249
- su(Hw)* suppressor, of hairy-wing protein, 33
- sup 7*, nematodes transgenic for, 247
- Supermouse, generation of, 165
- surgery, in transgenic bird preparation, 109
- SV40 virus
 in gene construct, 68, 76
 T antigen of, in transgenic mice, 149, 151–2

Index

265

- symbiont transformation for transfer, in insects, 42
- tag-and-exchange strategy, in site-specific genome recombination system, 168
- TATA boxes, 5–6
- Tay–Sachs disease, possible gene therapy of, 13
- teleosts, gene isolation from, 88
- terminal repeat sequences, in transgene integration, 7
- thalassaemias
 gene therapy of, 13
 transgenic mice use in studies of, 151
- thymidine kinase, as promoter, 140
- tilapia, *see Oreochromis niloticus*
- Ti* plasmid infection, gene transfer by, 24
- tissue plasminogen activator, expression by transgenic goats, 220
- tissue specific expression, transgenic animal use to study, 3
- tissue-specific locus control regions, regulation of gene expression by, 9–10
- Tk* gene
 in cell ablation studies, 84
 as marker gene, 147
 rodents transgenic for, 192
- tobacco, transgenic, 8
- tomatoes, transgenic, 17, 87
- toxins, transgenic induction of, 16, 17
- tra-3*, nematodes transgenic for, 247
- transactivators, in transgenic large mammals production, 185–6
- transcription factors, consensus sequence recognition by, 6
- transcription site interactions, transgenic animal use to study, 3
- transferases, as integration facilitators, 7
- transforming growth factor beta, in stem cell cultures of farm animals, 189
- transgenes
 definition of, 138
 direct tissue injection of, 12
 expression of, 3
 facilitating methods, 8–10
 factors affecting, 6
 regulation, 9
 transient expression, 8–9
 integration of, 3, 6
 detection techniques, 6
 expression, 9–10
 facilitating methods, 7
 single copy and concatemer tandem copies, 6
 introduction into animal, 6–7
 loss of, 2–3, 6, 8
 methylation of, 6
 microneedle injection of, 6–7
 transient, 6
 transmission of, 3, 5
 detection methods, 6
 optimization, 10–11
in vivo transfer of, 12
- transgenic animals
 books and reviews on, 4
 breeding of, 229–32
 definitions of, 1, 2, 138
 developments based on, 6–15
 early work on, 1
 as food, 15
 genetic engineering usage and, 3
 legislation affecting, 3
 as living test tubes, 3, 8
 methodology for, 4–6
 and moral issues, 15–16
 mosaicism in, 2, 5, 10
 pharmaceuticals from, 2, 14–15, 220
 possible interbreeding of, 18
 possible problems posed by, 18–19
 production of, 3–4
 release control of, 18–19
 selective breeding compared to, 1, 2
 transient, 2–3
- transgenic imprinting, genomic imprinting in, 158–9
- transgenic large mammals
 applications of, 180, 181
 gene farming of, 181
 methods of formation, 179–80
 alternative techniques, 194–5
 DNA microinjection, 179, 182–8
 embryonic stem cells, 180, 188–91
 sperm cell use, 179–80
 mutation analysis in, 179
- transmission-blocking vaccines, for malaria parasite, 53
- transposase
 gene for, of *Drosophila*, 7–8
 helper element for, 29
 sources for, 31, 34
 transposition in transgenic *Drosophila* by, 28
- transposon tagging
 in *Drosophila*, 22, 34–35, 48
 in mosquitoes, 44
- transresponders, in transgenic large mammal production, 185–6
- trout; *See also Oncorhynchus mykiss*
 gene isolation from, 87, 88, 89
 transgenic, gene constructs for, 90, 91, 92, 93
- trout growth hormone, in gene constructs, 93
- Trypanosoma brucei*, transfection of, 246

- Trypanosoma cruzi*, transfection of, 246
 trypanosomes, transgenic, 245, 246
 trypsin genes, from insects, 47
 Anopheles gambiae, 57
 tumor necrosis factor (TNF), gene coding for, 12–13
 tungsten particles, DNA-coated
 in biolistics method for insect gene transfer, 40
 gene transfer to fish eggs by, 66
 particle bombardment of egg, 5
 turkeys, chimeras of, 121
 tyrosinase gene
 in gene constructs, 92
 as marker transgene in transgenic fish, 68, 77, 85
- United Kingdom
 genetic engineering authorization in, 12, 16
 transgenic animal release control in, 18
 United States, genetic engineering authorization in, 12, 16
 upstream activation system, in regulation of mouse gene expression, 166
- vasotocin gene, isolation from fish, 88
 vasotocin precursor gene, 88
 vermilion *Drosophila* mutants, 23
 vermilion gene, as selectable marker for *Drosophila*, 30
- viruses, promoters from, 68
 vitellogenin gene, isolation from fish, 87
 v-myc gene, rodents transgenic for, 192
- whey acidic protein gene, in gene constructs for pigs, 209
 white gene, as selectable marker for *Drosophila*, 30
 winter flounder, gene isolation from, 87
 wool production, in transgenic sheep, 213–15
- Xenopus laevis*, transgenic, 73, 77, 114, 245, 250–1
 xenotransplantation, large transgenic mammal use for, 180, 181
Xiphophorus, gene isolation from, 87
- yeast, transgenic, 21, 87, 245
 yeast artificial chromosomes, in transgenic animal generation, 141–2, 186
 yellow-fin sea-bream, gene isolation from, 87
 yellow gene, as selectable marker for *Drosophila*, 30
- zebra fish, *see Brachydanio rerio*
 Z gene, as reporter gene, 6