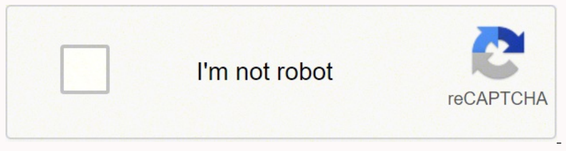

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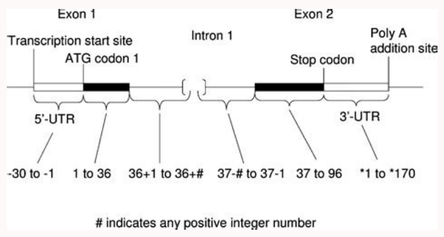
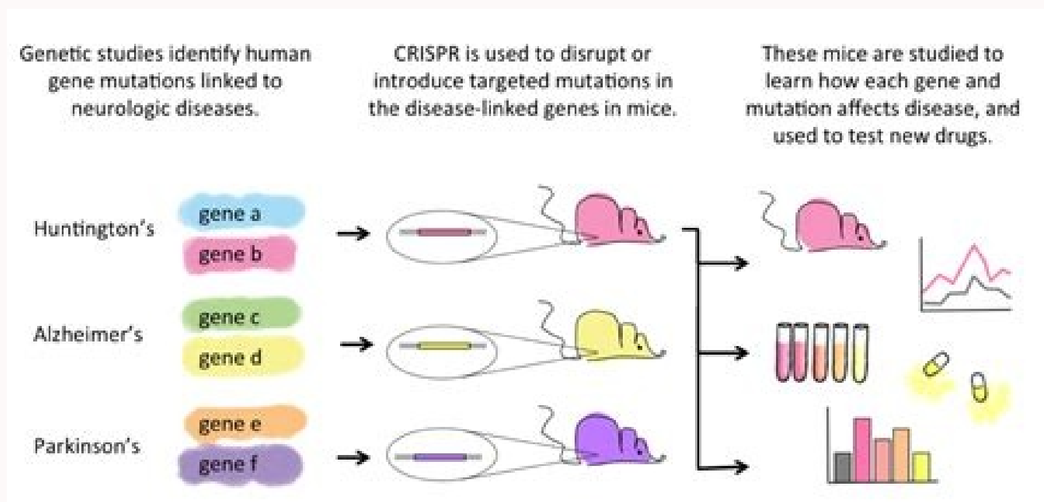
Genetic mutation nomenclature guide



Standard name	*lacZ*
Mnemonic	lactose Lactose
Synonyms	*ECK0341, b0344, JW0335*[1]
edit table	

Defect	Features
GnRH receptor gene mutations	Female phenotype: delayed puberty, variable thelarche, ***amenorrhea***; autosomal recessive inheritance
FSHβ gene mutations	Female phenotype: delayed puberty, absent thelarche, ***primary amenorrhea*** and infertility; autosomal recessive inheritance
FSHR gene mutations	Female phenotype: ***primary amenorrhea*** with variable development of secondary sex characteristics; autosomal recessive inheritance
LHβ gene mutations	Female phenotype: only LHβ polymorphisms have been identified to date, producing minimal, if any, negative effect in LH function; autosomal recessive inheritance
LHR gene mutations	Female phenotype: ***primary amenorrhea***, with normal development of secondary sex characteristics; the phenotype depends on the amount of



Gene name	No. of amplicons screened	Size screened (bp)	No. of mutations	Mutation frequency (Kb)
ADCL1	1	595	1	1/456.9
ADCS	2	1121	1	1/860.9
CCD4A	3	1728	8	1/165.8
CCD4B	2	1124	2	1/431.6
CHRC	3	1543	5	1/237.0
COP1	6	3368	10	1/258.6
CRTISO	1	593	0	–
CYCB	4	2212	5	1/339.7
DHFS	2	1167	3	1/298.7
$FPGS_M$	1	566	0	–
$FPGS_P$	2	1173	2	1/450.4
GCH1	2	1046	2	1/401.6
GGH1	2	1192	2	1/457.7
GGH2	1	599	0	–
GGH3	1	580	2	1/222.7
NCED1	4	1825	4	1/350.4
OR	2	1158	2	1/444.6
PAP3	1	592	0	–
PHYF	2	1018	1	1/781.8
PSY1	5	2882	4	1/553.3
SPA1	2	1273	0	–
SPA3	2	1041	3	1/266.4
SPA3LIKE	2	1150	5	1/176.6
TF	1	417	0	–
ZEP	1	600	2	1/230.4
Total	55	30 563	64	1/367

The designated reference sequence is that of C57Bl/6J strain. Examples: Plaur plasminogen activator, urokinase receptor Staautosomal striping be italicized in published articles. The characteristics of these loci are such that they are "benign" in not affecting expression or function of other genes. Protein symbols are not italicized. Laboratory codes can be assigned through MGD or directly by the Institute for Laboratory Animal Research (ILAR) at . 7 References Bestor TH. Note that although subtle alterations made in a gene appear to lend themselves to a simple naming convention whereby the base or amino acid changes are specified, in fact these do not provide unique gene names, as such alterations, which could be made in independent labs, while bearing the same changes, may differ elsewhere in the gene. Other features, such as alleles, variants and mutations, are secondary to the gene name and become associated with it. 2.10.2 Defining uniqueness in QTL Specific circumstances for naming independent QTL include: Independent experiments study the same trait and map that trait to the same chromosomal region Because QTL are detected in the context of specific strain combinations in specific crosses and generally in different laboratories using different assays, each experimentally detecting QTL will be given a unique symbol/name even when the trait measured and region defined is superficially the same as that of an existing QTL. In many cases, a large number of transgenic lines are made from the same gene construct and only differ by tissue specificity of expression. The use of allele symbols for DNA segments is mainly limited to describing inheritance and haplotypes in crosses. 2013. The same applies for rat DNA segments detected by cross-hybridization to mouse segments (or vice versa). Examples: C57BL/6J-Tg(CD8)1Jwgmouse strain C57BL/6J carrying the Tg(CD8)1Jwg transgene. Example: Tg(RP22-412K21)15Som a BAC transgene where the inserted BAC is from the RP22 BAC library, plate 412, row K, column 21. Serial numbers are independent for mouse and rat revertants and no homology is implied. Example: Cftrtm1Unc is the first targeted mutation of the cystic fibrosis transmembrane regulator (Cftr) gene produced at the University of North Carolina. Some historically named QTL carry the name of the disease with which they are associated; these names are maintained, but newly identified QTL should be named for the measured trait and not a disease. In: Genetic Variants and Strains of the Laboratory Mouse, Green, M.C. (ed.), First Edition, Gustav Fischer Verlag, Stuttgart, pp. 2.6.1 Families Identified by Hybridization Historically, many gene families have been identified as fragments detected by hybridization to the same probe but which map to different loci. Transgenic symbols should be submitted to MGD or RGD through the nomenclature submission form for new loci. Example: Tfamtm1Lrsn and Tfamtm1.1Lrsn. The assay must show genetic variation of the marker to map the locus on a genetic map but not to place it on a physical map. In general a

transposable element concatamer marker will already be established, as above. BALB/cHeA) 3.4 Insertional and Induced Mutations Mutations that are induced, targeted, or selected in structural genes are named as alleles of the structural gene. Committee on Standardized Genetic Nomenclature for Mice. Thus one or more alternative protein products can be produced by a single allele of a gene. Examples: Slc11a1rsolute carrier family 11, host resistance allele Slc11a1ssolute carrier family 11, host susceptibility allele (the QTL originally known as BCG/Lsh resistance has been identified as Slc11a1) Scc2BALB/cHeA colon tumor susceptibility 2, BALB/cHeA allele Scc2STS/Acolon tumor susceptibility 2, STS/A allele(for QTL Scc2, the STS/A allele has increased tumor susceptibility vs. 2.4.3 Opposite Strand Genes Transcripts from the opposite strand that overlap another gene, or a transcript that is derived principally from the introns of another gene, or one that uses an alternative reading frame to another gene (and does not use the existing frame to a significant extent) should be given a different name. Example: awgTg(GBtslenv)832Pkw this mutation of abnormal wobbly gait is caused by a transgene in mouse line 832, produced in the laboratory of Paul Wong. Where a gene becomes assigned to a gene family (of paralogs), and the nomenclature of the family is established. 6.15 Ortholog Genes in different species are orthologs if they have evolved from a single common ancestral gene. Names and symbols of new members of these families should follow the rules of the particular family and ideally be assigned in consultation with the curator of that family. 1-7. Penetrance is a quantitative measure of how often the phenotype occurs in a population; and expressivity is a measure of how strongly a phenotype is expressed in an individual. However, letter order in a gene symbol need not follow word order in the name. Even if the identified gene is novel and unnamed, it is recommended that it is nevertheless given a name and symbol different from the mutant name and symbol. (c.f. Gaj, et al., 2013; Wijshake, et al., 2014) Endonuclease-mediated mutations are given the symbol of the mutated gene, with a superscript consisting of three parts: the symbol "em" to denote an endonuclease-mediated mutation, a serial number from the laboratory of origin and the ILAR registered laboratory code of the laboratory where the mutation was produced. While the gene name should ideally be informative as to the function or nature of the gene, care should be taken to avoid putting inaccurate information in the name. In 2003, the International Committee on Standardized Genetic Nomenclature for Mice and the Rat Genome and Nomenclature Committee agreed to unify the rules and guidelines for gene, allele, and mutation nomenclature in mouse and rats. Family member numbers or subunit designations should be placed at the end of the gene symbol. If different Rnr loci can be genetically identified on the same chromosome, they are given serial numbers in order of identification. The mouse or rat strain on which the transgene is maintained should be named separately as in the Rules and Guidelines for Nomenclature of Mouse and Rat Strains. For example, the beta globin genes of mouse, rat and human are orthologs. Desvignes T, Batzel P, Berezikov E, Eilbeck K, Eppig JT, McAndrews MS, Singer A, Postlethwait JH. These synonyms may be associated with the gene in databases and publications, but the established gene name and symbol should always be used as the primary identifier. Other types of variants include differences in protein molecular weight or charge, differences in enzyme activity, or differences in single-stranded conformation (SSCP). 1992. In tables of genotypes, the gene symbol can be omitted and the allele abbreviation used alone. A chromosomal region containing many measured "traits" If multiple traits are measured in a single experiment and mapped to a single chromosomal region, there may or may not be evidence that different QTL are involved. 54:159-162. One utility of these transgenes is in creating cre driver lines. If there is evidence that any loci are pseudogenes, they should be named as such and given serial numbers as in Section 2.6.2. Once sequence evidence is accumulated on functional family members (which may or may not have been previously identified as members) a systematic naming scheme should be applied to the family as in Section 2.6.2. 2.6.2 Families Identified by Sequence Comparison Sequencing can identify genes that are clearly members of a family (paralogs). For sex chromosomes, use of "X Chromosome" or "Y Chromosome" is accepted. Dupuy AJ, Akagi K, Largaespada DA, Copeland NG, Jenkins NA. MGI (for mouse) or RGD (for rat) should be consulted for the next available cluster number when a new cluster is defined. A dominant phenotype is detectable when only one variant allele is present. Biochem. Information on these families can be found at family-specific web sites, some of which are linked from MGD and RGD. In these cases, the foreign (replacing) gene symbol is used parenthetically as part of the targeted allele symbol. The format then is Genemutation+tm#Labcode Example: Crb1rd8+em1Mvw reversion to wild-type of the Crb1rd8 mutation by endonuclease mediated targeting, 1st reported from the laboratory of Michael Wiles. 6.4 Marker A marker is the means by which a gene or a locus is identified. By contrast, a gene modified by targeting at the endogenous locus is an allele and should be named as such. 6.13 Haplotype A haplotype is the association of genetically linked alleles, as found in a gamete. However, in some cases, such as when homologous recombination is used to target a gene, a readily identified phenotype may not result even though the gene may be rendered non-functional. Details of the targeted locus should be given in associated publications and database entries. Within a gene symbol, Laboratory codes have an initial uppercase letter When describing cross-hybridizing DNA segments, H (human) or other species code is uppercase, for example D2H11S14. A DNA segment that maps within an HSR is given a conventional DNA segment symbol, when its locus is on a normal (unamplified) chromosome. A single mutation may confer both a dominant and a recessive phenotype. 2.9 Gene Trap Loci Gene trap experiments in embryonic stem (ES) cells produce cell lines in which integration into a putative gene is selected by virtue of its expression in ES cells. A web tool for proposing a new mouse locus symbol is located at the MGD site. 2.8 Anonymous DNA Segments Only anonymous DNA segments that are mapped should be given systematic names and symbols. Situations where hyphens may be used include: to separate related sequence and pseudogene symbols from the root histocompatibility gene loci Examples: Fpr-rs6formyl peptide receptor, related sequence 6 H2-Ab1 histocompatibility 2, class II antigen A, beta 1 within superscripted allele symbols (Section 3.1.2) Example: Kit W-v Kit oncogeneallele name: viable dominant spotting within transgene symbols to separate promoter and expressed sequences (Section 4) Example: Tg(Drd2-EGFP)S118Gsat transgene insertion S118, GENSAT Project at Rockefeller University 2.3.2 Gene Names Names of genes should be brief, and convey accurate information about the gene. In general, pseudogenes result from either reverse transcription of a transcript of their "normal" paralog (in which case the pseudogene typically lacks introns and includes a poly(A) tail; often called processed pseudogenes) or from recombination (in which case the pseudogene is typically a tandem duplication of its "normal" paralog). Examples: Gt(DTM030)Bygfor a trapped gene (at an undefined locus) in mutant ES cell line DTM030, made by BayGenomics Osbpl1aGt(OST48536)Lex gene trap allele of the oxysterol binding protein-like 1A gene, in mutant ES cell line OST48536, made by Lexicon Genetics, Inc. 3.2 Variants 3.2.1 Biochemical Variants Electrophoretic or other biochemicalvariant alleles of known structural genes are usually given lowercase letters to indicate different alleles, and in the symbol the letter becomes a superscript to the gene symbol. 1.5.2 Protein symbols Protein designations follow the same rules as gene symbols, with the following two distinctions: Protein symbols use all uppercase letters. Examples: In mouse, recessive spotting, rs; abnormal feet and tail, Aft; circling, cir Further (allelic) mutations at the same locus, if they have the same phenotype, are given the same name with a Laboratory code preceded by a serial number (if more than one additional allele from the same lab). Note that genes are either homologous or not; there are no degrees of homology! For example, all globin genes, and myoglobin, are homologs, even though some are more closely related to each other than others. Strictly speaking, even direct determination of DNA variants is assaying phenotype not genotype as it is dependent on a particular assay, although it is so close to genotype that it serves as a surrogate. If a second heritable allele was then generated after mating with a cre transgenic mouse, it would retain the parental em# designation followed by a decimal point and serial number. 6.16 Paralog Paralogous genes are genes within the same species that have arisen from a common ancestor by duplication and subsequent divergence. Even if the phenotype is apparently identical, the original symbol is used, with the new mutation symbol as superscript. Examples: Wt1 Wilms tumor 1 homolog Acly ATP citrate lyase use American spelling not contain punctuation, except where necessary to separate the main part of the name from modifiers, or if a comma is part of a protein name. The existence of a gene can also be inferred in the absence of any genetic or physical map information, such as from a cDNA sequence. HGVS Recommendations for the Description of Sequence Variants: 2016 Update. Examples: D4Mit17DNA segment, Chr 4, Massachusetts Institute of Technology 17 (a simple sequence length polymorphism within the mouse Orm1 gene) D20Wox3 DNA segment, Chr 1, Wellcome Trust Oxford 3 (a simple sequence length polymorphism within the rat Tnf gene) Mouse or rat DNA segments that are detected by cross-hybridization to human segments are given the human name with "chromosome N, cross-hybridizing to human DNA segment" inserted between DNA segment and the human segment code (see symbols). Cell 122:473-483. However, certain cytological features of normal chromosomes (such as telomeres, centromeres, and nucleolar organizers) and abnormal chromosomes (such as homogeneously-staining regions and end-points of deletions, inversions, and translocations) are genetic loci that are given names and symbols. A single gene may have several loci within it (each defined by different markers) and these markers may be separated in genetic or physical mapping experiments. Transgenes containing RNAi constructs can be designated minimally as: Tg(RNAi:geneX)#Labcode, where geneXis the gene that is knocked down #is the serial number of the transgene An expanded version of this designation is: Tg(Pro-yyRNAi:geneX)#Labcode, where Pro- can be used optionally to designate the promoter yy can be used optionally for the specific RNAi construct While there is the option to include significant information on vectors, promoters, etc. Wurst laboratory. Revertant to wild type of the dilute mutation of myosin Va; Myo5ad+ Second such revertant identified at The Jackson Laboratory; Myo5ad+2J Engineered reversions of phenotypic mutations should be indicated by the gene symbol and superscripted mutant symbol followed by the + symbol and appropriate engineered allele designation. For example, Hc14 is the pericentric heterochromatin on Chromosome 14. The gene name or symbol should not include the name mouse or any abbreviation such as the letter "M" for mouse or the name rat or any abbreviation such as the letter “R” for rat. The new allele, then, will be a superscripted form of the concatamer symbol. Endonucleases: new tools to edit the mouse genome. The same family members in different mammalian species (orthologs) should, wherever possible, be given the same name and symbol. Bear in mind that identification of a variant or mutant phenotype is recognition of an allelic form of an as-yet unidentified gene that may already have or will be given a name. F344/CrlBR-Tg(HLA-B*2705, B2M)33-3Trg rat strain F344/CrlBR carrying the Tg(HLA-B*2705,B2M)33-3Trg double transgene For BAC transgenics, the insert designation is the BAC clone and follows the same naming convention as the Clone Registry at NCBI. Gaj T, Gersbach CA, Barbas CF 3rd. Committee on Standardized Genetic Nomenclature for Mice, Chairperson: Davisson, M.T. 1996. are not part of the enhancer trap nomenclature. 2.11.4 Homogeneously Staining Regions Homogeneously staining regions (HSRs) are amplified internal subchromosomal bands that are identified cytologically by their Giemsa staining. If the mutation is shown to be a deletion of all or part of the structural gene, the superscript del can be used in place of m. Knock-in alleles expressing RNAi under the control of the endogenous promoter can be designated using targeted mutation or transgene mutation nomenclature, as appropriate: Example: When a targeting vector is used to generate multiple germline transmissible alleles, such as in the Cre-Lox system, the original knock-in of loxP would follow the regular tm designation rules. It is the 15th in the mouse made in the laboratory of Stefan Somlo (Som). Targeted mutations that result in the ablation of any gene expression (i.e., functionally null) are termed knock-out mutations. A recessive phenotype is one that is only detected when both alleles have a particular variant or mutation. The series is separate for mouse and rat and no homology should be implied by the serial numbers. The most recent publication of mouse nomenclature guidelines can be found in Eppig (2006). Examples: In mouse, Nidd1 (non-insulin-dependent diabetes mellitus 1) was associated with related measurements of plasma insulin, non-fasted blood glucose, and body weight and given a single QTL designation. It may refer to single genes or loci or to many. This causes the transposable-element to come in contact with the transposase and to be mobilized from its original site, and, when reintegrated into the genome, can cause a heritable phenotypic mutation. A gene name should: be specific and brief, conveying the character or function of the gene begin with a lowercase letter, unless it is a person's name or is a typically capitalized word. Examples: l4Jus24 lethal, Chr 4, Justice 24 l1Rk8 lethal, Chr 1, Roderick 8 2.6 Gene Families Genes that appear to be members of a family should be named as family members. 1-11. Other, secondary, functions of nomenclature for genes are to: identify the gene as a member of a family, which may give further information about the gene by reference to other family members identify the gene as the ortholog of a gene in another mammal (usually human) 1.2 Definitions It is important that the user understands what is being named and the principles underlying these guidelines. For example, a targeted allele created by Velocigene (Regeneron) in the KOMP knockout project: Gstm3tm1(KOMP)Vlcg Once fully designated in a publication, the allele can be abbreviated by removing the portion of the allele designation in parentheses (in this case, Gstm3tm1Vlcg), provided the symbol remains unique. The chromosomal designation for mitochondrial genes is Chr MT. (c.f., Ding, et al.,2005; Bestor, 2005; Dupuy, et al., 2005). Rules and guidelines for genetic nomenclature in mice. Wijshake T, Baker DJ, van de Sluis B. Report of the committee on mouse genetics nomenclature. In such cases, it is useful to define these different loci, but normally the gene name should be used to designate the gene itself, as this usually will convey the most information. For example, the mouse patch (Ph) mutation has a heterozygous (dominant) pigmentation phenotype but also a homozygous (recessive) lethal phenotype. Enhancer traps of this type that are currently being created may include a minimal promoter, introns, a cre recombinase cassette (sometimes fused with another element such as ERT2), and polyA sites from different sources. When expanded into an HSR its symbol follows the guidelines for insertions, thus becoming, for example, Is(HSR;1)1Lub. These might be clone end-fragments, inter-repeat sequence PCR products, or random sequences from within clones. Many allelic variants, in particular DNA variants, do not confer any external phenotype on the animal. In most cases, the alleles should be named according to their strain of origin and symbolized by adding the strain abbreviation as superscript, although for resistance and sensitivity, variants r and s may be used. Example: In mouse, Obq1 (obesity QTL 1) was identified and mapped to Chromosome 7 in a cross between strains 129/Sv and EL/Suz. These variants are often termed “polymorphisms” although, strictly speaking, that term applies only to variants with a frequency of more than 1% in the population. Generally, the number and effects of QTL can only be deduced following experiments to map them. Laboratory codes are also used in naming chromosomal aberrations, transgenes, and genetically engineered mutations. 4.1 Symbols for transgenes It is recognized that it is not necessary, or even desirable, to name all transgenes. Eppig, JT. Soriano's laboratory, is Gt(ROSA)26Sor. Read-through transcript genes should be named with a unique symbol and name. Genet. Transgenes, which are not part of the native genome, are not italicized. In describing a transgenic mouse or rat strain, the strain name should precede the transgene designation. pp.79-98. For example, the mouse alpha globin and beta globin genes are paralogs. The mutation is introduced during homology-directed or non-homologous end-joining repair of the induced DNA break(s). Nomenclature guidelines are now reviewed and updated annually by the two International Committees; current guidelines can be found on the MGD and RGD web sites. The general format of the symbol is: Tg(promoter-transposase)#Labcode Example: Tg(ACTB-sb10)545Abc The symbol consists of: Tg denoting transgene In parentheses, the official gene symbol for the promoter, using the nomenclature of the species of origin, followed by a hyphen and a lowercase transposase symbol, in this case sb10 for the Sleeping Beauty 10 transposase The laboratory's line or founder designation or a serial number The Laboratory code of the originating lab For a targeted knock-in of the transposase, use the standard format for a targeted mutation, i.e., the symbol of the targeted gene with a superscripted allele symbol beginning with the prefix tm. Therefore, pseudogenes are generally assigned the next number or letter in the relevant gene family symbol series. If the traits are physiologically related, the QTL name should be broad enough to represent all the measured traits or the name should reflect the trait showing the highest LOD score/p-value. These family members may be functional genes or pseudogenes. Mamm. Once the mutant gene product is identified, the gene product is given a name and symbol and the original phenotype-based symbol and name becomes the allele symbol and name. Examples: Park2rs6200232-G The Park2 rs6200232 SNP allele with the G variant Park2rs6200232-AThe Park2 rs6200232 SNP allele with the A variant If the SNP occurs outside of an identified gene, the SNP locus can be designated using the dbSNP_ID as the locus symbol and the nucleotide allelic variants are then superscripted as alleles. Example: Fgf1em1Mcw the first endonuclease-induced mutation of the fibroblast growth factor 1 (Fgf1) gene produced at the Medical College of Wisconsin When an endonuclease genome editing technology is used to generate multiple germline transmissible alleles, such as in the Cre-Lox system, the original knock-in of loxP would follow the regular em# designation guidelines. Additional details for naming mutations and visualizing allele structures for targeted mutations generated from the International Knockout Mouse Consortium (IKMC) are provided separately. Example: mouse ornithine decarboxylase-related sequences 1 to 21.Odc-rs1 to Odc-rs21 If the founder or functional gene can not be identified, initially all the fragments are named "related sequence" until it is identified; then that particular "-rs" is dropped, without renumbering. For example, a "liver-specific protein" may be shown by subsequent studies to be expressed elsewhere. The transgene symbol is made up of four parts: Tg denoting transgene In parentheses, the official gene symbol of the inserted DNA, using nomenclature conventions of the species of origin The laboratory's line or founder designation or a serial number (note that numbering is independent for mouse and rat series) The Laboratory code of the originating lab No part of a transgene symbol is ever italicized as these are random insertions of foreign DNA material and are not part of the native genome. In: Genetic Variants and Strains of the Laboratory Mouse, Lyon, M.F., A.G. Searle (eds.), Second Edition, Oxford University Press, Oxford, pp. The SV40 large T antigen is another example. Examples: D16H21S13Mouse DNA segment on Chr 16 that cross-hybridizes with a DNA segment D21S13 from human Chr 21 D1M7Mit236 Rat DNA segment on Chr 1 that cross-hybridizes with a DNA segment D7Mit236 from mouse Chr 7 2.8.2 STSs Used in Physical Mapping When physical maps are assembled (YAC or BAC contigs, for example) many markers may be placed on the map in the form of Sequence Tagged Sites (STSs). Naming microRNA clusters A microRNA cluster consists of several microRNAs in immediate genome proximity. 2.15 Long noncoding RNAs Long non-coding RNAs (long ncRNAs, lncRNAs) are defined as transcripts longer than 200 nucleotides that are not translated into protein. 1.5.3 Chromosome designations Use uppercase "C" when referring to a specific mouse chromosome (e.g., Chromosome 15) for autosomal chromosomes. D11Mit19a, D11Mit19b, D11Mit19c are variant alleles of D11Mit19 in mouse. For example, an assay that detects variation of DNA or protein will almost invariably detect codominant inheritance, as both alleles are detected. These markers differ from Regulatory Region markers in that Igs# loci do not exhibit regulator function. in 1995. Until the molecular nature of a functional mammalian centromere is defined, DNA segments that map to the centromere should be given anonymous DNA segment symbols as in Section 2.8.1. Pericentric heterochromatin, that is cytologically visible, is given the symbol Hc#, in which # is the chromosome on which it is located. J. Examples: In rat, calmodulin pseudogenes 1 and 2, Calm-ps1 and Calm-ps2 In mouse, phosphoglycerate kinase 1a to 1d, Pgk1a to Pgk1d In mouse, Ces2a, Ces2b, Ces2c, Ces2d1, Ces2e, Ces2f, Ces2g, Ces2h Members of the carboxylesterase 2 gene family, where Ces2d1 appears as a unique entity in the series of named carboxylesterase 2 family members Numerous gene families have been recognized and given systematic nomenclature. Help is available for determining correct gene and allele symbol assignment (nomen@jax.org) and symbols can be reserved privately pre-publication. However, a particular allele may be found in several inbred strains, and, furthermore, it may be difficult to establish whether an allele in one strain is identical to one in another. 1963. They may be a combination of any type of markers, and may extend over large, genetically separable distances, or be within a short distance such as within a gene and not normally separated. Cd19tm1(cre)Cgn in this targeted knock-in mutation, cre was inserted in-frame in exon 1. 3.5.4 Enhancer Traps Enhancer traps are specialized transgenes. (see Section 2.6.2). 1940. Examples of this type of variation include levels of metabolite, immune response to antigen challenge, viral resistance, or response to drugs. Rules and guidelines for gene nomenclature. 6.17 Cluster A cluster is a group of genomic entities located in close proximity to each other on a chromosome. Different transgenic constructs containing the same gene should not be differentiated in the symbol; they will use the same gene symbol in parentheses and will be distinguished by the serial number/Laboratory code. 3.5.2 Endonuclease-mediated Mutations Endonuclease-mediated mutations are targeted mutations generated in pluripotent or totipotent cells by an endonuclease joined to sequence-specific DNA binding domains. These genes are given the root symbol Rnr and the number of the chromosome on which they are located. Because the measured traits are independent, different QTL designations are assigned. For example, the 26th gene "trapped" by the ROSA vector in the laboratory of Phillip Soriano (Sor) is symbolized as: Except for the above case, the gene trap designation becomes an allele of the gene into which it was inserted, once that gene is identified. 2014 Apr 30 for example, Mod1a-m1Lws is a mutation of the mouse Mod1a allele, the first found in the laboratory of Susan Lewis. Genotype can only be determined by assaying phenotype, including test mating to reveal carriers of recessive mutations. As the terms are applied to phenotypes not to genes or alleles, then in the case where a gene has multiple mutant alleles, each can confer a phenotype that is dominant to some, but recessive to other, phenotypes due to other alleles. These markers serve to validate the contigs and appear on the maps, but their further utility may be limited. Exceptions to the rule of uppercase first letter and lowercase remaining letters in a gene or locus symbol: If the gene (locus) is only identified by a recessive mutant phenotype, then the symbol should begin with a lowercase letter. In this case, each of the alleles A, B, and C by definition must differ in their DNA sequence. Information about the nature of the transgenic entity should be given in associated publications and database entries. These should retain the accepted nomenclature features of other alleles of that class. Example: Tg(TCF3/HLF)1Mlc a transgene in which the human transcription factor 3 gene and the hepatic leukemia factor gene were inserted as a fusion chimeric cDNA, the first transgenic mouse line produced by Michael L. 2.11 Chromosomal Regions Separate documents detail guidelines for nomenclature of chromosomes (for mouse, Rules for Nomenclature of Chromosome Aberrations are online; for rat, see Levan, et al., 1995). For MHC complex engineered alleles, include the haplotype of the allele symbol, similar to spontaneous mutations. Reporter symbols, however, are not indicated in allele symbols. Naming microRNAs Symbols for microRNAs consist of the root symbol Mir followed by the numbering scheme tracked in the miRBase database (www.mirbase.org), a database tracking microRNAs reported for all species. An example is diagrammed below. Trends Biotechnol 31: 397-405. The allele names and symbols should be the same as those used for the phenotype. If multiple sequence sources are available for the novel gene, preference is given first to a RIKEN clone ID then a BC clone ID (from Mammalian Gene Collection). Note that examining the database content for a QTL is not sufficient, as a laboratory may have a QTL designation reserved and private, pending publication. Rules and guidelines for gene nomenclature. Levan G., H.J. Hedrich, E.F. Remmers, T. For high throughput systematic gene trap pipelines, the mutant ES cell line's designation can be used in parentheses instead of the vector designation, and the serial number following the parentheses may be omitted. When a measure of relatedness between sequences is required, percent identity or similarity should be used. The Mouse Genome Database (MGD) serves as a central repository of gene names and symbols to avoid use of the same name for different genes or use of multiple names for the same gene ( ). The allele expresses cre recombinase specifically in B-lineage cells throughout development. 2.11.3 Nucleolus Organizers The nucleolus organizer is a cytological structure that contains the ribosomal RNA genes. In addition, they can be localized far away from the gene(s) that they affect. For example, if a number of transgenic lines are described in a publication but not all are subsequently maintained or archived, then only those that are maintained require standardized names. Genes that are known to be pseudogenes in any mouse strain are given a strain specific marker biotype note that includes strain-specific functional information. Inheritance is usually assayed in genetic crosses, but identification of the gene in cytogenetic or physical maps are other means of mapping the locus of a gene. Examples: D8Mit17DNA segment, Chr 8, Massachusetts Institute of Technology 17 D1Arb27 DNA segment, Chr 1, Arthritis and Rheumatism Branch, NIAMS The same convention is applied to DNA segments that are variant loci within known genes. 2.8.1 Mapped DNA Segments Anonymous DNA segments are named and symbolized according to the laboratory identifying or mapping the segment as "DNA segment, Chromosome N, Lab Code" and a serial number, where N is the chromosomal assignment (1-19, X, Y in the mouse and 1-20, X, Y in the rat) and is symbolized as DNLabcode#. 3.2.3 Single Nucleotide Polymorphisms (SNPs) Polymorphisms defined by SNPs may occur within or outside of a protein coding sequence. If the trapped gene is known, the symbol for the trapped allele will be similar to a targeted mutation of the same gene using the format Gt(vector content)#Labcode for the allele designation. Genomic Variants could refer to nuclear or organellar genomes. The human protein is expressed from this allele and the endogenous mouse protein is undetectable. A revision of the standardized genetic nomenclature for mice. All mutant alleles, whether of spontaneous or induced origin, targeted mutations, gene traps, or transgenics should be submitted to MGD (mouse) or RGD (rat) for an allele or gene accession identifier. Because they may be difficult to read, depending on the browser, gene symbols are frequently not italicized when posted to a web page use a common stem or root symbol when belonging to a gene family. The Laboratory Code of the lab originating the transposable element line If a newly transposed insertion occurs in an unknown site or intergenic region, the form: Tn(transposon_class_abbreviation-vector)#Labcode is used to symbolize the "genomic mutation" without being superscripted to a gene symbol, similar to the way a random transgene inserted into a non-gene site is designated. In such cases, the targeted genes are nevertheless referred to as mutant alleles. This section describes the guidelines for naming the inserted transgene. Tfamtm1Lrsn designates another germline transmissible allele generated after mating with a cre transgenic mouse. The general format of the symbol is: Genetm#(transposase)Labcode Example: Gt(ROSA)26Sortm1(sb11)Njen The symbol consists of: The gene into which the transposase was integrated, in this case Gt(ROSA)26Sor In the superscript: tm denoting targeted mutation A serial number of the targeted mutation In parentheses, a lowercase transposase symbol, in this case sb11 for the Sleeping Beauty 11 transposase The Laboratory Code of the originating lab 5.3 Transposed Insertion Alleles These alleles follow the rules for naming all other alleles. Where there is only a single locus on a chromosome, the chromosome anomaly symbol serves to define it. Usually these are markers described by statistical association to quantitative variation in the particular phenotypic traits that are controlled by the cumulative action of alleles at multiple loci. Genetic variation may also produce phenotypic variation in morphology, behavior, or other observable traits that interact in a complex manner with other genes and/or with the environment. Examples: rs6200616T A SNP locus with the T variant rs6200616CA SNP locus with the C variant Note: If a gene Xyz is later discovered to include this SNP locus, rs620061, then the alleles listed above become Xyzrs620061-T and Xyzrs620061-C. To see previous versions of these guidelines (last revised in December 2015), click here. Examples: Tg(Wnt1-LacZ)206Amc the LacZ transgene with a Wnt1 promoter, from mouse line 206 in the laboratory of Andrew McMahon Tg(Zp3-cre)3Mrtthe cre transgene with a Zp3 promoter, the third transgenic mouse line from the laboratory of Gail Martin In the case of a fusion gene insert, where roughly equal parts of two genes compose the construct, a forward slash separates the two genes in parentheses. 3.5 Targeted and Trapped Mutations 3.5.1 Knock-out, Knock-in, Conditional and Other Targeted Mutations Mutations Mutations that are the result of gene targeting in ES cells are given the symbol of the targeted gene, with a superscript consisting of three parts: the symbol tm to denote a targeted mutation, a serial number from the laboratory of origin and the Laboratory code where the mutation was produced (see Section 2.1). Examples: H2-Kb-tm1Bpe targeted mutation allele on 129P2/OlaHsd b haplotype H2-Db-tm1Bpe targeted mutation allele on 129P2/OlaHsd b haplotype H2-Ab1g7-em1Ygch CRISPR generated allele on NOD g7 haplotype Large-scale projects that systematically produce a large number of alleles (>1000) may include a project abbreviation in parentheses as part of the allele designation. 3.1 Mutant Phenotypes 3.1.1 Genes Known Only by Mutant Phenotypes Where a gene is known only by mutant phenotype, the gene is given the name and symbol of the first identified mutant. Mouse Genome 92 vii-xxxii. Bear in mind that resistance alleles deriving from different strains may not be the same and should be given different names and symbols. 2.1 Laboratory Codes A key feature of mouse and rat nomenclature is the Laboratory Registration Code or Laboratory code, which is a code of usually three to four letters (first letter uppercase, followed by all lowercase), that identifies a particular institute, laboratory, or investigator that produced, and may hold stocks of, for example, a DNA marker, a mouse or rat strain, or were the creator of a new mutation. This new allele should be named as described in Section 3.4.2. The transgene itself is a new genetic entity for which a name may be required. 5.1 Transgenic Transposable Element (TE) Concatamers The transgenic transposable element concatamers are identified with a standard prefix Tg (for transgenic) and Tn (for transposable element). (An abbreviated form, awgTg832Pkw can be used if the abbreviated designation is unique.) If the additional allele has a different phenotype, it may be given a different name, but when symbolized the new mutant symbol is superscripted to the original mutant symbol. These guidelines, therefore, are intended to aid the scientific community as a whole to use genetic information. The following method symbolizes these nuclear-encoded RNA genes: Naming nuclear encoded transfer-RNAs Symbols for nuclear encoded transfer-RNAs consist of four parts: n- lowercase n followed by a hyphen to indicate nuclear encoding T uppercase T to indicate transfer-RNA A the single letter abbreviation for the amino acid (uppercase) xxx the 3-letter anticodon (lowercase) # serial number (only when needed to distinguish multiple copies of a particular anticodon tRNA class Example: n-TAagc12 nuclear encoded tRNA alanine 12 (anticodon AGC) Naming nuclear encoded ribosomal-RNAs Symbols for nuclear encoded ribosomal-RNAs consist of four parts: n- lowercase n followed by a hyphen to indicate nuclear encoding R uppercase R to indicate ribosomal-RNA subunit the subunit designation # serial number for this ribosomal-RNA Example: n-R5s104 nuclear encoded rRNA 5S 104 2.14 microRNAs and microRNA clusters MicroRNAs (miRNAs) are abundant, short RNA molecules that are post-transcriptional regulators that bind to complementary sequences on target mRNA transcripts, usually resulting in translational repression or target degradation and gene silencing. This scheme is to name the transgene entity only. Examples: En1tm1(Otx2)Wrst in this targeted knock-in mutation, the coding region of En1 was replaced by the Otx2 gene, originating from the W. Cleary's laboratory (Mlc). Accepted nomenclature for the transposable-element inserts, transposase transgenes, and resulting transposed insertion alleles are given below. Notes: This term currently includes the following variant types: substitution, point mutation, insertion, deletion, insertion and deletion. When genetically inherited variants of a gene or locus are detectable by any means, the different alleles enable genetic mapping. 6.11 Phenotype Phenotype is the result of interaction between genotype and the environment and can be determined by any assay. 2014. A gene symbol should: be unique within the species and should not match a symbol in another species that is not a homolog. 2.5.1 Lethal Phenotypes Genes identified solely by a recessive lethal phenotype with no heterozygous effect are named for the chromosomal assignment, a serial number and the name of the laboratory of origin (from the Laboratory code). 6.1 Gene A gene is a functional unit, usually encoding a protein or RNA, whose inheritance can be followed experimentally. The trapped gene is usually (though not necessarily) mutated by the integration. However, the difference between allele B versus alleles A and C must include a sequence difference that affects the splicing pattern of the gene. Thus, it is misleading to name them based on the gene for which regulation was first recognized. Note: somatic events generated in offspring from a Tfamtm1Lrsn bearing mouse and a cre transgenic that cause disruption of Tfam in selective tissues would not be assigned nomenclature. 3.5.3 Gene Trap Mutations Gene trap mutations are symbolized in a similar way to targeted mutations. 6.2 Pseudogene A sequence that closely resembles a known functional gene, at another locus within a genome, that is non-functional as a consequence of (usually several) mutations that prevent either its transcription or translation (or both). 9:369-374. In these cases the relevant nomenclature for transgenes or targeted mutations is used. The list of microRNAs included in each cluster will be recorded in relevant database records for the genes, knockouts, and strains. Among different alleles, alternative splice forms may or may not differ, depending on whether the sequence difference between the alleles affects the normal splicing mechanism and results in differences in the exon (or partial exon) usage. 1-16. The primary purpose of a gene or locus name and symbol is to be a unique identifier so that information about the gene in publications, databases and other forms of communication can be unambiguously associated with the correct gene. Also, if a new mutation is described and named but not shown to be an allele of an existing gene until later, the original name of the new mutation can be kept. The fine molecular detail of these loci and mutations should reside in databases such as MGD and RGD. The sequence difference occurs at a single position or in contiguous nucleotides. The following Guidelines were developed by an interspecies committee sponsored by ILAR in 1992 and modified by the Nomenclature Committee in 1999 and 2000. If the SNP occurs within a gene, the SNP allele can be designated based on its dbSNP_ID, followed by a hyphen and the specific nucleotide. 6.9 Dominant and Recessive Dominant and recessive refer to the nature of inheritance of phenotypes, not to genes, alleles, or mutations. ILAR News 34:S1-S56. Note that all such alleles that are "derived from" a transposable element concatamer carry the original number with a decimal point and serial number identifying the specific allele. Apoetm1(APOE*2)Mae in this targeted knock-in mutation, a DNA fragment containing exons 2-4 of a human APOE2 isoform replaced the equivalent portion of the mouse Apoe gene. Examples: Tg(Zfp38)D1Htza transgene containing the mouse Zfp38 gene, in line D1 reported by Nathaniel Heintz. Examples: A4galt alpha 1,4-galactosyltransferase Zfy1 zinc finger protein 1, Y-linked include the name of the species from which the ortholog/homolog name was derived at the end of the name in parentheses only when that name is not in common usage. The contents of the parentheses will usually be the symbol for the transposase with which it is associated. Conversely, if there is clear evidence that the traits are independent, each trait will constitute a unique QTL. Guidelines for nomenclature of genetically determined biochemical variants in the house mouse, Mus musculus. miRNA Nomenclature: A View Incorporating Genetic Origins, Biosynthetic Pathways, and Sequence Variants. Examples: mt-TctRNA, cysteine, mitochondrial(a tRNA gene residing on the mitochondria) mt-Atp6 ATP synthase 6, mitochondrial (a non-tRNA gene residing on the mitochondria) 2.13 RNA Housekeeping Genes Encoded in the Nucleus There are hundreds of loci encoding transfer RNAs (tRNA) and ribosomal RNAs (rRNA), and many are encoded in the nucleus. The general format of the symbol is: TgTn(transposon_class_abbreviation-vector)#Labcode Example: TgTn(sb-T2/GT2/tTA)1Dla The symbol consists of: Tg denoting transgenic Tn denoting transposon In parentheses, a lowercase abbreviation of the transposon class (in this case sb for Sleeping Beauty), followed by a hyphen and the vector designation The laboratory's line or founder designation or a serial number The Laboratory Code of the originating lab 5.2 Transposase Inserts Transposases can be engineered into the genome via transgenesis or specific gene targeting. Intergenic sites are to be symbolized as: Igs# Intergenic site # where # indicates the next number in the series. Details describing specific of knock-in constructs should be associated in databases or publications, and not in nomenclature. When a definitive human ortholog exists, gene names should also agree with human gene names when practical. Rules for rat genetic nomenclature were first published by the Committee on Rat Nomenclature in 1992 and then by Levan et al. 2.7 ESTs Expressed Sequence Tags (ESTs) differ from other expressed sequences in that they are short, single pass sequences that are often convenient for PCR amplification from genomic DNA. Examples: Shhsonic hedgehog [commonly used, does not include species name] Ssu2 ssu-2 homolog (C. The end points of each of these rearrangements, however, define a locus. Technologies generating these types of mutations include TALENs, CRISPR, Cas9, etc. 6.5 Allele The two copies of an autosomal gene or locus on the maternal and paternal chromosomes are alleles. 1.4 Synonyms A gene can have several synonyms, which are names or symbols that have been applied to the gene at various times. When abbreviating the word Chromosome, do not use a period (".") after the abbreviation (e.g., Chromosome 15 should abbreviated as Chr 15 and not Chr.15). The MGD Nomenclature Committee (nomen@jax.org) provides advice and assistance in assigning new names and symbols. 3.4.2 Transgenic Insertional Mutations Mutations produced by random insertion of a transgene (not by gene targeting) are named as a mutant allele of the gene (which should be given a name and symbol if it is a novel gene), with the superscript the symbol for the transgene (see Section 3.1.1 for examples, and Section 4 for naming transgenes). Hered. For example, Rnr19-1, Rnr19-2. Nomenclature schemes and curation of new families benefit from examination of existing models. To distinguish between mRNA, genomic DNA, and cDNA forms within a manuscript, write the relevant prefix in parentheses before the gene symbol, for example, (mRNA) Rbp1. These intergenic genomic sequences can be modified by targeted, spontaneous or other means of mutagenesis to facilitate the creation of alleles for modified intergenic sites such as those generated by MICER targeting or knock-out alleles for highly conserved sequences that reside within intergenic sequences. It is accepted that the name may not cover all aspects of the phenotype; what is needed is a succinct, memorable and, most importantly, unique, name. Other genes on the opposite strand should be assigned the symbol of the known gene with the suffix "os" for opposite strand. Mammalian mutagenesis using a highly mobile somatic Sleeping Beauty transposon system. These are molecular details of the specific construct that will be captured in database records and reported with experimental results. Nomenclature for these enhancer traps consists of 4 parts as follows: Et prefix for enhancer trap cre recombinase cassette portion in parentheses...for example, cre, icre, or cre/ERT2 (if fused with ERT2) line number or serial number to designate lab trap number or serial number Lab code ILAR code identifying the creator of this enhancer trap Examples: Et(icre)1642Rdav Enhancer trap 1642, Ron Davis Et(cre/ERT2)2047Rdav Enhancer trap 2047, Ron Davis Note that the minimal promoter, poly A source, etc. A DNA segment that includes the telomere repeat sequence (TTAGGG)n and which maps to a telomeric location is symbolized in four parts: Tel (for telomere) The number of the chromosome p or q (for the short or long arm, respectively) A serial number, if more than one segment is assigned to the telomere For example, Tel4q1 telomeric repeat sequence, Chr4, q arm 1 2.11.2 Centromeres and Pericentric Heterochromatin The functional centromere should be denoted by the symbol Cen. ESTs that clearly derive from a known gene should be considered simply as an assay (marker) for that known gene. 2006. If a gene is later discovered to include this SNP locus, the same guidelines are applicable as those used when mutant locus symbols become alleles of known genes. Definition, nomenclature, and conservation of rat strains. The loci of integration of a series of gene trap lines, once characterized as potentially unique, can be named and symbolized as members of a series, using the prefix Gt (for gene trap), followed by a vector designation in parentheses, a serial number assigned by the laboratory characterizing the locus, and the laboratory ILAR code. The hotfoot (ho) mutation of the mouse glutamate receptor Grid2, Grid2ho The dominant white spotting (W) mutation of mouse Kit, KitW If the original mutation has multiple alleles, when describing these alleles, their symbols become part of the superscript to the identified structural gene. If the two alleles are identical, the animal is homozygous at that locus. Specifically for a QTL, its name should include: a root name describing the measured trait the designation QTL (recommended) a serial number Examples: in mouse Cafq1caffeine metabolism QTL 1 Cafq2caffeine metabolism QTL 2 Cafq3 caffeine metabolism QTL 3 in ratKidm1kidney mass QTL 1 Kidm2kidney mass QTL 2 Kidm3 kidney mass QTL 3 To obtain the next available serial number for a new QTL with an already established root name, e.g., the next in the series of "liver weight QTL" in mouse (Lwq#) or the next in series of "blood pressure QTL" for rat (Bp#), users should submit their QTL on the "proposing a new locus symbol" form at MGD (for mouse) or RGD (for rat). The gene should as far as possible be given the same name as the protein, whenever the protein is identified. 5 Transposon-induced Mutations and Inserts Three types of genetic inserts are involved in creating transposon-induced mutations. Trends Genet 31: 613-626. elegans) [name includes species derivative] NOT include the word mouse (for a mouse gene name) or the word rat (for a rat gene name) follow the conventions of the established gene family if it is a recognizable member of that family by sequence comparison, structure (motifs/domains), and/or function not contain potentially misleading information that may be experiment or assay specific, such as "kidney-specific" or "59 kDa" 2.4 Structural Genes, Splice Variants, and Promoters Ultimately, the majority of gene names will be for structural genes that encode protein. Cell 122:322-325. 6.8 Mutation A mutation is a particular class of variant allele that usually confers a phenotypically identifiable difference to a reference "wild type" phenotype. The general format is: GeneTn(transposon_class_abbreviation-vector)#Labcode Example: Car12Tn(sb-T2/GT2/tTA)1.1Dla The symbol consists of: The gene into which the transposable element was integrated (transposed) In the superscript: Tn denoting transposon In parentheses, a lowercase abbreviation of the transposon class (in this case sb for Sleeping Beauty), followed by a hyphen and the vector designation A serial number, in which the primary number corresponds to that given to the transposable element concatamer from which it arose, followed by a decimal point and a serial number designating its number within the series of derivative insertion alleles. Particularly in segregating crosses, or where there is a threshold effect on phenotypic manifestation, these measures provide additional ways to describe how particular allelic combinations result in a phenotype. When anonymous ESTs are mapped onto genetic or physical maps, their designations should be symbolized using their sequence database accession number. The contents of the parentheses will usually be the promoter and the symbol for the transposase with which it is associated, separated by a hyphen. For the rat, these functions are carried out by RGD ( ) assisted by the International Rat Genome and Nomenclature Committee (RGNC). Committee on Standardized Genetic Nomenclature for Mice, Chair: Lyon, M.F. 1981. Where possible, members of the family should be named and symbolized using the same stem followed by a serial number. Standardized rat genetic nomenclature. Note that in mouse and rat, a gene may be a pseudogene in one inbred strain but not another. 4 Transgenes Any DNA that has been stably introduced into the germline of mice or rats is a transgene. 6.7 Splice Variant or Alternative Splice Alternative splicing of a gene results in different, normally occurring forms of mRNA defined by which exons (or parts of exons) are used. In: Fox J, Barthold S, Davvison M, Newcomer C, Quimby F, Smith A (eds) The Mouse in Biomedical Research, Volume 1, Second Edition. Taurog. These genes can only be identified by virtue of allelic variation. 3.4.1 Mutations of Structural Genes Variants of structural genes that are clearly mutations, whether or not they confer a phenotype, are given the superscript m#Labcode, where # is a serial number and is followed by the Laboratory code where the mutation was found or characterized. When no information is available, other than the sequence itself, use the sequence identifier from the Mammalian Gene Collection, RIKEN, or GenBank (e.g., AF067061, 0610009F21Rik). be short, normally 3-5 characters, and not more than 10 characters use only Roman letters and Arabic numbers begin with an uppercase letter (not a number), followed by all lowercase letters / numbers (see exception below) not include tissue specificity or molecular weight designations include punctuation only in specific special cases (see below) ideally have the same initial letter as the initial letter of its gene name to aid in indexing. Example: Zbtb8os zinc finger and BTB domain containing 8, opposite strand 2.4.4 Genes with Homologs in Other Species To aid interspecific comparison of genetic and other information, a gene that is identifiable as a homolog/ortholog of an already-named human gene should be given the same name and symbol as the human gene, where possible. If the STSs are used more widely, they should be assigned anonymous DNA segment names ("D-numbers"). QTL should not be named until such mapping experiments have been performed. However, where an anomaly gives two loci on a single chromosome they can bedistinguished by the letters p and d for proximal and distal. For a transgene, use the standard prefix Tg (for transgene). If a second heritable allele was then generated after mating with a cre transgenic mouse, it would retain the parental designation followed by a decimal point and serial number. 6 Definitions The following definitions should aid the user in understanding what is being named, and in understanding the principles underlying these guidelines. For example, In(1)1Rk-p, In(1)1Rk-d are the proximal and distal end points of the chromosomal inversion In(1)1Rk in mouse. The most common of these are transgenes that use reporter constructs or recombinases (e.g., GFP, lacZ, cre), where the promoter should be specified as the first part of the gene insertion designation, separated by a hyphen from the reporter or recombinase designation. Another obesity QTL was also mapped to Chromosome 7, but because it involved distinct strains (NZO and SM), it was given a different QTL designation, Obq15. For example, Hc14n is normal heterochromatin; superscripts l and s would be used to denote long and short heterochromatin, respectively. 1.3 Stability of Nomenclature On the whole gene names should be stable; that is, they should not be changed over time. Serikawa, M.C. Yoshida. 2005. Genome 6:447-448. See also the examples of gene trap mutations in Section 3.5.2. 2.10 Quantitative Trait Loci, Resistance Genes, and Immune Response Genes Differences between inbred strains and the phenotype of offspring of crosses between strains provide evidence for the existence of genes affecting disease resistance, immune response, and many other quantitative traits (quantitative trait loci, QTL). For example, allele A may produce mRNAs of splice form 1, 2, and 3; while allele B may produce mRNAs of splice form 1, 2, and 4; and Allele C may produce mRNAs of splice form 1, 2, and 3. Gordon. 6.6 Allelic Variant Allelic variants are differences between alleles, detectable by any assay. Committee on Standardized Genetic Nomenclature for Mice, Chair: Lyon, M.F. 1989. Those QTL affecting the same trait should be given the same stem and serially numbered. Example: tp2J the second new allele of the taupe gene identified at The Jackson Laboratory If a new allelic mutation of a gene known only by a mutant phenotype is caused by a transgenic insertion, the symbol of this mutation should use the symbol of the transgene as superscript (see Section 3.4.2 and Section 4). Where orthologous gene(s) have been identified between mouse, rat, and human, and a common symbol is adopted for all three species. For example, differences in anonymous DNA sequences can be detected as simple sequence length polymorphism (SSLP) or single nucleotide polymorphisms (SNPs). The suffix "q" may be used optionally as the final letter preceding the serial number in QTL symbols. Known pseudogenes should be assigned a serial number. The recessive nature of the allele is still conveyed by an initial lowercase letter. Evidence for QTL is generally obtained through extensive genetic crossing and analysis that may uncover many genetic elements contributing to a phenotypic trait. If a mouse gene model is available from NCBI or ENSEMBL, a Gm (gene model) symbol is used. Dunn, L.C., H. If the mutation is known to have occurred on a particular allele, that can be specified by preceding the superscript with the allele symbol and a hyphen. The symbol is usually an abbreviation for the inbred strain in which the variant is being described. As long as the symbols are defined in the description, users are free to use whatever allele symbol best fits their needs. In rats, Uae5 (urinary albumin excretion QTL 5) and Cm16 (cardiac mass QTL 16) are QTLs derived from the same experiment that map to overlapping regions of Chromosome 1. den Dunnen JT, Dalgleish R, Maglott DR, Hart RK, Greenblatt MS, McGowan-Jordan J, Roux AF, Smith T, Antonarakis SE, Taschner PE (2016). Transposons reanimated in mice. The conservation of long ncRNAs is assessed on a case by case basis. ZFN, TALEN, and CRISPR/Cas-based methods for genome engineering. 2.3 Gene Symbols and Names 2.3.1 Gene Symbols Genes are given short symbols as convenient abbreviations for speaking and writing about the genes. The use of promoter designations is helpful in such cases. Never prepend 'm' (for a mouse gene symbol) or 'r' (for a rat gene symbol) to indicate species. Examples: Glra1 glycine receptor alpha 1 Glra2 glycine receptor alpha 2 Glra3 glycine receptor alpha 3 use the same symbol whenever possible for orthologs among human, mouse and rat. Symbols of mutations conferring a recessive phenotype begin with a lowercase letter; symbols for dominant or semidominant phenotype genes begin with an uppercase letter. Other more complex forms of gene replacement, such as partial "knock-in", hit-and-run, double replacements, and loxP mediated integrations are not conveniently abbreviated and should be given a conventional tm#Labcode superscript. A web tool for proposing a new rat locus symbol is located at the RGD site. 2015. Targeted mutations, in which a foreign gene or gene segment is inserted into a target gene, resulting in expression of the foreign gene under control of the endogenous promoter are termed knock-in mutations. In general, these sites are benign, not affecting expression or function of other genes, but can act as a generic site for many kinds of inserted DNA. When a definitive human ortholog exists, gene symbols should agree with human gene symbols when practical. Similarly, probes or assays used to detect a gene are not primary features and should not normally be used as names. Section 2 below specifies naming rules for establishing correct gene symbols. For transfer RNAs, the symbols consist of three parts, mt-, T (for tRNA), and a single lowercase letter for the amino acid. Novel mutant phenotypes or traits should be named according to their primary characteristic, but once the gene responsible for the phenotypic variation is identified, this gives the primary name of the gene and the mutant name becomes the name of the allele (see Section 2.3). 6.3 Locus A locus is a point in the genome, identified by a marker, which can be mapped by some means. creeper, Grid2ho-cpr. Example: grey coat is an allele of recessive spotting (rs) in the mouse, and hence is symbolized rsgrc 3.1.2 Phenotypes Due to Mutations in Structural Genes When a spontaneous or induced mutant phenotype is subsequently found to be a mutation in a structural gene, or the gene in which the mutation has occurred is cloned, the mutation becomes an allele of that gene and the symbol for the mutant allele is formed by adding the original mutant symbol as a superscript to the new gene symbol. Mouse Strain and Genetic Nomenclature: an Abbreviated Guide. In this example, Tfamtm1Lrsn designates a targeted mutation where loxP was inserted into the Tfam gene. Evidence of gene families comes in a variety of forms, but is principally based on sequence comparisons. (c.f. Desvignes, et al., 2015) For example, mouse Mir143 (microRNA 143) is represented as mmu-mir-143 in miRBase, with the mmu signifying mouse. 6.12 Quantitative Trait Loci (QTLs) Quantitative Trait Loci (QTL) are polymorphic loci that contain alleles, which differentially affect the expression of continuously distributed phenotypic traits. In the case of sequences, care should be taken in interpretation of database searches to establish novelty (for example, to distinguish between a new member of a gene family and an allele or alternative transcript of an existing family member). 2.4.2 Read-through Transcripts A read-through transcript is a multi-exon transcript that shares one of more exons with non-overlapping shorter transcripts that are considered to represent products of distinct loci. 2.11.5 Chromosomal Rearrangements Symbols for chromosomal deletions, inversions, and translocations are given in the Rules for Nomenclature of Chromosome Aberrations. within the parentheses of a transgene symbol, this should be minimized for brevity and clarity. Enhancers, promoters, and regulatory regions are to be symbolized as: Rr#regulatory region # where # indicates the next number in the series 3 Names and Symbols for Variant and Mutant Alleles Different alleles of a gene or locus can be distinguished by a number of methods, including DNA fragment length, protein electrophoretic mobility, sequence comparison, or variant physiological or morphological phenotype. Section 6 presents definitions that will aid the user in distinguishing, for example, genes, loci, markers, and alleles. 2.4.1 Alternative Transcripts Alternative transcripts that originate from the same gene are not normally given different gene symbols and names. The wild type allele of the taupe mutation, tp+ The wild type Kit locus (if necessary to distinguish from mutations), Kit+ A revertant to wild type of a mutant phenotype locus should be indicated by the symbol + with the mutant symbol as superscript. The loci can be named "related sequence" of the founder gene with a serial number (symbol -rs1, -rs2, and so on). It is not necessary to give them names or symbols other than those assigned by the laboratory that produced and used them. 1995. Tg(HLA-B*2705, B2M)33-3Trg a double transgene in rat containing the human HLA-B*2705 and B2M genes, that were co-injected, giving rise to line 33-3 by Joel D. Nature 436:221-226. International Committee on Standardized Genetic Nomenclature for Mice, Chairperson: Davisson, M.T. 1994. 2.12 Genes Residing on the Mitochondria The mitochondria carry essential genes, among them many transfer RNA (tRNA) genes. However there are certain circumstances where a change is desirable: In cases where a gene has been known only as, and named for, a mutant phenotype: when the mutated gene is identified, then the mutant name becomes the mutant allele name of the identified gene (see Section 3.1.2). The *, as used in the last example above, indicates that the included gene is mutant. This is usually readily recognized as a distinct pattern, not to be confused with simple alternate splicing for a locus. Because Laboratory codes are key to identifying original sources, they are not assigned to "projects," but rather to the actual producer/creator individual or site. Committee on Rat Nomenclature, Cochairmen Gill T.J. III, Nomura T. Ding S, Wu X, Li G, Han M, Zhuang Y, Xu. T. In particular, a transgene inserted randomly in the genome is not an allele of the endogenous locus; the condition is termed hemizygous if the transgene is present only in one of the two parental chromosome sets. These may be given symbols and names to refer unambiguously to the entire cluster. 2.11.1 Telomeres The functional telomere should be denoted by the symbol Tel. 2.10.1 Names and Symbols of QTL Names and symbols for QTL should be brief and descriptive and reflect the trait or phenotype measured. For a microRNA cluster, the name will consist of the root symbol Mirc (for microRNA cluster) followed by a serial number (1, 2, 3...) for the cluster. Thus, in miRBase clusters defined based on one miRNA may or may not overlap clusters based on another miRNA. The site of integration can be characterized by a number of means, including cloning or extension of cDNA products. The function of a symbol is to provide a unique designation to a gene, locus, or mutation. 6.10 Genotype Genotype is the description of the genetic composition of the animals, usually in terms of particular alleles at particular loci. The name should not convey detailed information about the gene or assay used; this can be associated with the gene in publications or databases. To refer to specific splice forms of a gene, the following format should be used (gene symbol, followed by underscore, followed by sequence accession ID): Genesymbol_accID Example: Gene Mttpmicrosomal triglyceride transfer protein Splice variant Mttp_EU553486 microsomal triglyceride transfer protein splice variant defined by transcript sequence EU553486 Using the sequence accession ID provides an unambiguous and precise definition to the splice variant. For example, Gt(ST629)Byg is known to disrupt the netrin 1 (Ntn1) gene; thus the full allele designation for this gene trap mutation is Ntn1Gt(ST629)Byg. Variation in heterochromatin band size can be denoted by superscripts to the symbol. Use of hyphens within the symbol should be kept to a minimum. 4.2 Intergenic sites used as "neutral" recipient sequence landing sites Commonly used insertion sites include Gt(Rosa)26Sor and Hprt. Serial numbers are independently assigned in mouse and rat and the same assigned serial number does not imply orthology. 2 Symbols and Names of Genes and Loci The prime function of a gene name is to provide a unique identifier. For example, a gene trapped locus (where the gene is unknown) using vector ROSA, the 26th made in P. (Note that this differs from the definition of miRBase, which simply refers to clustered miRNAs as those less than 10kb from the miRNA of interest. In most cases, there will not be a clear wild type; hence all alleles should be named. Naming and symbolizing QTL follow the same conventions as for naming and symbolizing genes (Section 2.3). If the revertant is in a gene that has been cloned, then the mutant symbol is retained as superscript to the gene symbol, and + is appended. 31:505-506. Two lines, one carrying the transposable-element as a concatamer and the other carrying the transposase are mated. Examples: JThe Jackson Laboratory MitMassachusetts Institute of Technology LehHans Lehrach KyoKyoto University Ztm Central Animal Laboratory Medical School Hannover 2.2 Identification of New Genes Identification of new genes in general comes in two ways; identification of a novel protein or DNA sequence or identification of a novel phenotype or trait. See IKMC mutation nomenclature and IKMC allele structure. 2.5 Phenotype Names and Symbols Genes named for phenotypes should aim to convey the phenotype briefly and accurately in a few words. Gruneberg, G.D. Snell. 1973. Example: glucose phosphate isomerase 1 alleles a and b; Gpi1a, Gpi1b 3.2.2 DNA Segment Variants Variants of DNA segments are indicated by a superscript to the symbol. 6.14 Homolog Genes are homologous if they recognizably have evolved from a common ancestor. For example, Rnr12 is the ribosomal RNA locus on Chromosome 12. Example: Akap12Gt(ble-lacZ)15Brr a gene trap allele of the Akap12 gene, where the gene trap vector contains a phleomycin resistance gene (ble) and lacZ, the 15th analyzed in the laboratory of Jacqueline Barra (Brr) If the trapped gene is novel, it should be given a name and a symbol, which includes the letters Gt for "gene trap," the vector in parentheses, a serial number, and Laboratory code. If a mutation produces a phenotype in the heterozygote that is intermediate between the homozygous normal and mutant, the phenotype is referred to as semidominant. Note that the numbering of pseudogenes among species is independent and no relationship should be implied among mouse, rat, or human pseudogenes based on their serial numbering. New sites that are intergenic are being identified that can also serve as neutral insertion sites for transgenesis and are designated by Igs# (Intergenic site #), where # indicates a serial number. A single chromosome can only carry a single allele and, except in cases of duplication, deletion or trisomy, an animal carries two autosomal alleles. Academic Press. Once the gene underlying a quantitative trait has been cloned or identified, the phenotypic name should be replaced by the name of the identified gene. (The mutant symbol should retain its initial upper or lowercase letter). Note that this should be used only for deletions that encompass a single gene; larger deletions should use the chromosomal deletion nomenclature. 1.5 Gene symbols, proteins, and chromosome designations in publications 1.5.1 Gene and allele symbols Gene symbols are italicized when published, as are allele symbols. Transgenes can be broken down into two categories: Those that are produced by homologous recombination as targeted events at particular loci Those that occur by random insertion into the genome (usually by means of microinjection) Nomenclature for targeted genes is dealt with in Section 3.5. Random insertion of a transgene in or near an endogenous gene may produce a new allele of this gene. HGVS style nomenclature may be used to describe the variant itself but not the allele: 3.3 Variation in Quantitative Trait Loci and in Response and Resistance Genes Variation in genes that do not give rise to a visible phenotype may be detected by assaying physiological or pathological parameters. "Cluster/region" is a marker type which encompasses clusters and regions such as histone, homeobox, olfactory receptor and other clusters; and cytochrome P450, histocompatibility 2, tumor suppressor and other regions. Users should be advised, however, that this web version represents the current nomenclature policies of the International Committee for Standardized Genetic Nomenclature for Mice and takes precedent over previously published versions. Guidelines for Nomenclature of Genes, Genetic Markers, Alleles, and Mutations in Mouse and Rat Revised: September, 2021 Chairperson: Dr. Cynthia Smith (e-mail:nomen@jax.org) Rat Genome and Nomenclature Committee Chairperson: Dr. Stanley Laulederkind Rules for mouse genetic nomenclature were first published by Dunn, Gruneberg, and Snell (1940) and subsequent revisions published by the International Committee for Standardized Genetic Nomenclature in Mice (1963, 1973, 1981, 1989, 1996). Tg(CD8)1Jwga transgene containing the human CD8 gene, the first transgenic line using this construct described by the lab of Jon W. The marker is dependent on an assay, which could, for example, be identification of a mutant phenotype or presence of an enzyme activity, protein band, or DNA fragment. Efficient transposition of the piggyBac (PB) transposon in mammalian cells and mice. This will more readily allow discrimination between mutant and wild type and between gene and phenotype. Hum Mutat 37(6):564-569. In the symbol the Laboratory code is added as a superscript. Biochim Biophys Acta. Lincmd1 for long intergenic non-protein coding RNA of muscle differentiation 1 Xist for X inactive specific transcript 2.16 Enhancers, Promoters, and Regulatory Regions Enhancers, promoters, and regulatory regions can influence multiple genes. Note that several genes in the mouse or rat may have a single ortholog in another species and vice versa. In: Genetic Variants and Strains of the Laboratory Mouse, Lyon, M.F., Rastan, S., Brown, S.D.M. (eds.), Third Edition, Volume 1, Oxford University Press, Oxford, pp. viable white spotting, KitW-v; sash, KitW-sh. If both alleles can be simultaneously detected by an assay, then they are codominant. Rules and guidelines for gene nomenclature. If the gene is recognizable by sequence comparison as a member of an established gene family, it should be named accordingly (see Section 2.6). Table of Contents

Genes 3.4.2 Transgenic Insertional Mutations 3.5 Targeted and Trapped Mutations 3.5.1 Knockout, Knockin, Conditional and Other Targeted Mutations 3.5.2 Endonuclease-mediated Mutations 3.5.3 Gene Trap Mutations 3.5.4 Enhancer Traps 4 Transgenes 4.1 Symbols for transgenes 4.2 Intergenic insertion sites used as "neutral" recipient sequence landing sites 5 Transposon-induced Mutations and Inserts 5.1 Transgenic Transposable Element (TE) Concatamers 5.2 Transposase Inserts 5.3 Transposed Insertion Alleles 6 Definitions 6.1 Gene 6.2 Pseudogene 6.3 Locus 6.4 Marker 6.5 Allele 6.6 Allelic Variant 6.7 Splice Variant or Alternative Splice 6.8 Mutation 6.9 Dominant and Recessive 6.10 Genotype 6.11 Phenotype 6.12 Quantitative Trait Loci (QTLs) 6.13 Haplotype 6.14 Homolog 6.15 Ortholog 6.16 Paralog 6.17 Cluster 7 References 1 Principles of Nomenclature 1.1 Key Features The key component of nomenclature is the gene or locus name and symbol, which identifies a unit of inheritance. 3.1.3 Wild Type Alleles and Revertants The wild type allele of a gene is indicated by + as superscript to the mutant symbol. Examples: Ptpn6em1.1Shoy the first derivative of the first endonuclease-induced mutation of the protein tyrosine phosphatase, non-receptor type 6 gene produced by Sho Yamasaki Gt(ROSA)26Sorem1.1(CAG-cas9*,-EGFP)Rsky the first derivative of the first endonuclease-induced mutation of the gene trap ROSA 26 gene produced by Klaus Rajewsky Any CRISPR-generated allele is always an em. 3.2.4 Genomic Variant Definition (from Alliance of Genome Resources): A DNA sequence that differs relative to a designated reference sequence. Revertant to wild type at the hairless mutant locus +hr Additional revertants are given a Laboratory Code and preceded by a serial number if more than one revertant is found in a lab. Genes residing on the mitochondria have a prefix mt- (lowercase mt followed by a hyphen). It has been shown that functional activity of a gene that has a pseudogene designation can occur in different mouse and rat strains. It does not necessarily correspond to a gene; it could, for example, be an anonymous non-coding DNA segment or a cytogenetic feature. The class of transposable element may be included in parentheses.

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