Nomenclature for mutant alleles generated in ES cell lines by the International Knockout Mouse Consortium (IKMC)

The goal of the IKMC is to mutate all protein-coding genes in the mouse using gene trapping and gene targeting in C57BL/6N-derived ES cells. This document specifies the allele nomenclature for this subset of mouse gene mutations. For the complete guidelines for naming genes, alleles, and mutations, visit the Guidelines for Nomenclature of Genes, Genetic Markers, Alleles, and Mutations in Mouse and Rat.

There were 5 primary classes of mutant alleles produced by the IKMC (all in ES cell lines). In addition, targeted cre knockin alleles are being made in conjunction with IKMC by the EUCOMMtools project.

1. Gene Trapped Alleles
2. Targeted Reporter-tagged Deletion Alleles
3. Targeted Knockout First, Reporter-tagged Insertion with Conditional Potential (conditional-ready)
4. Targeted Knockout First, Reporter-tagged Insertion NON-conditional
5. Targeted Knockout First Alleles with Artificial Introns
6. Targeted cre Knockin Alleles

In some cases, derivative alleles can be generated from the primary mutant allele. Nomenclature for derivative forms is also described below. Schematics of the molecular structure of IKMC alleles are shown on this page.

Symbols and Names for IKMC alleles

IKMC Abbreviations

Nomenclature Abbreviations	IKMC Project	Associated Laboratory Codes
KOMP	Knockout Mouse Project (KOMP, USA)	Mbp, Wtsi, Vlcg
EUCOMM	European Conditional Mouse Mutagenesis (EUCOMM) & EUCOMMMtools (Europe)	Hmgu, Wtsi

NCOM	North American Conditional Mouse Mutagenesis (NorCOMM, Canada)	Cmhd, Mfgc
TIGM	Texas A & M Institute for Genomic Medicine (TIGM)	Tigm

1. Gene Trapped Alleles.

Symbols for gene trapped alleles follow the format: Gene-symbol$^{\text{Gt(mutant cell line ID)Labcode}}$

The allele symbol has a superscripted portion comprised of:

Gt	gene trap
(cell line ID)	enclosed in parentheses, the mutant ES cell line ID
Labcode	the laboratory code for the institution or investigator creating the allele.

Examples:	*Rnd3*$^{Gt(IST12405G10)Tigm}$	Rho family GTPase 3; gene trap IST12405G10, Texas A&M Institute for Genomic Medicine
	Nmnat2$^{Gt(EUCE0262a08)Hmgu}$	nicotinamide nucleotide adenylyltransferase 2; gene trap EUCE0262a08, Helmholtz Zentrum Muenchen GmbH

Depending on the gene trap design (e.g., inclusion of FRT and loxP sites), some gene trapped alleles can be used to create **derivative alleles** through appropriate recombinase mediated changes.

Such derivative alleles for gene traps are symbolized in their superscripted portion by:

Gt	gene trap
(cell line ID)	enclosed in parentheses, the mutant ES cell line ID
1.#	derivative indication, 1 (for original) and .# for serially designated derivatives
Labcode	the laboratory code for the institution or investigator who created the original allele (not the lab code of the investigator/institution developing the derivative).

Example derivative gene trapped allele:

Nmnat2$^{Gt(EUCE0262a08)1.1Hmgu}$ nicotinamide nucleotide adenylyltransferase 2;gene trap EUCE0262a08, 1.1, Helmholtz Zentrum Muenchen GmbH

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2. Targeted Reporter-tagged Deletion Alleles.

These alleles follow the same nomenclature as all targeted alleles, with the exception that, because these alleles were generated in a large mutagenesis program, a project designation is given in parentheses. The format for these deletion alleles is:

Gene-symbol$^{tm\#(project\ abbreviation)Labcode}$

The allele symbol has a superscripted portion comprised of:

tm#	tm for targeted mutation, followed by a serial number
(project)	enclosed in parentheses, the project abbreviation
Labcode	the laboratory code for the institution or investigator creating the allele.

Examples: *Arrb2*$^{tm1(KOMP)Vlcg}$ arrestin, beta 2; targeted mutation 1, Velocigene

Mdk$^{tm1(KOMP)Mbp}$ midkine; targeted mutation 1, Mouse Biology Program, UCDavis

Derivative alleles. In the IKMC projects, two cassettes variations were inserted into the deleted genes:

(A) One included a LacZ reporter and a loxP-flanked neomycin cassette (Vlcg lab code).
(B) The other also included two FRT sites in the arrangement: FRT - LacZ – loxP – neo – FRT - loxP (Mbp and Wtsi lab codes).
Both types of tm1 alleles can generate a tm1.1 derivative allele through cre excision, which will remove the neo cassette from the locus. The designation for the cre-excised deletion allele changes the tm# portion of the allele symbol to tm#.1

Examples: *Arrb2*$^{tm1.1(KOMP)Vlcg}$ arrestin, beta 2; targeted mutation 1.1, Velocigene

Mdk$^{tm1.1(KOMP)Mbp}$ midkine; targeted mutation 1.1, Mouse Biology Program, UCDavis

The second variation (Mbp and Wtsi lab codes) allows another derivative allele to be created using, instead, flp-mediated excision. This excision removes both LacZ and neo

from the locus. This derivative allele changes the tm# portion of the allele symbol to tm#.2

Example: *Mdk*$^{tm1.2(KOMP)Mbp}$ midkine; targeted mutation 1.2, Mouse Biology Program, UCDavis

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3. Targeted Knockout First, Reporter-tagged Insertion with Conditional Potential (conditional-ready).

These alleles may contain a promoter or be promoterless. In the promoter-driven version, a critical exon is flanked by loxP sites, with upstream elements including FRT – LacZ – loxP – neo – FRT. Further allele modification is possible with cre- or flp-mediated recombination (see derivative alleles below). The format for these conditional-ready alleles is:

Gene-symbol$^{tm\#a(project\ abbreviation)Labcode}$

The allele symbol has a superscripted portion comprised of:

tm#a	tm for targeted mutation, followed by a serial number and an ‘a’ indicating an allele of the ‘knockout first, conditional-ready’ type
(project)	enclosed in parentheses, the project abbreviation
Labcode	the laboratory code for the institution or investigator creating the allele.

Example: *Cc2d1a*$^{tm1a(KOMP)Mbp}$ coiled-coil and C2 domain containing 1A; targeted mutation 1a, Mouse Biology Program, UCDavis

Derivative alleles of three types can be created from this allele by mating with mice carrying cre or flp recombinase or by expressing recombinase directly in ES cells, as follows:

1. Gene-symbol$^{tm\#b(project\ abbreviation)Labcode}$ is created when the original ‘tm1a’ allele undergoes cre-mediated recombination, which removes the neo and the critical exon.

   The allele symbol has a superscripted portion comprised of:

tm#b	tm for targeted mutation, followed by a serial number and a ‘b’ indicating that neo and the critical exon are removed creating a true knockout mutation
(project)	enclosed in parentheses, the project abbreviation
Labcode	the laboratory code for the institution or investigator who created the *original* allele (not the lab code of the investigator/institution developing the derivative).

Example: *Pipox*$^{tm1b(EUCOMM)Wtsi}$ pipecolic acid oxidase; targeted mutation 1b, Wellcome Trust Sanger Institute

2. Gene-symbol$^{tm\#c(project\ abbreviation)Labcode}$ is created when the original ‘tm1a’ allele undergoes flp-mediated recombination, which removes the LacZ reporter, a loxP site, and neo, leaving an intact gene with loxP flanking the critical exon. This allele can then be used for future cre-mediated conditional mutagenesis.

   The allele symbol has a superscripted portion comprised of:

tm#c	tm for targeted mutation, followed by a serial number and a ‘c’ indicating an allele suitable for conditional mutagenesis, where the LacZ and neo are removed and the gene is left inact, flanked by loxP sites around the critical exon(s)
(project)	enclosed in parentheses, the project abbreviation
Labcode	the laboratory code for the institution or investigator who created the *original* allele (not the lab code of the investigator/institution developing the derivative).

   Example: *Zfp260*$^{tm1c(NCOM)Mfgc}$ zinc finger protein 260; targeted mutation 1c, Mammalian Functional Genomics Centre

3. Gene-symbol$^{tm\#d(project\ abbreviation)Labcode}$ is created when the tm1c allele undergoes cre-mediated recombination, which removes the critical exon(s), leaving behind a single FRT and a single loxP site.

   The allele symbol has a superscripted portion comprised of:

tm#d	tm for targeted mutation, followed by a serial number and a ‘d’ indicating that the critical exon(s) are removed, with only one FRT and one loxP site remaining
(project)	enclosed in parentheses, the project abbreviation

Labcode	the laboratory code for the institution or investigator who created the *original* allele (not the lab code of the investigator/institution developing the derivative).
Example: *B9d1*$^{tm1d(EUCOMM)Wtsi}$	B9 protein domain 1; targeted mutation 1d, Wellcome Trust Sanger Institute

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4. Targeted Knockout First, Reporter-tagged Insertion NON-conditional.

These alleles are the same as those described above for the **tm1a** type allele, except that they have lost the loxP site downstream of the critical exon, so they are no longer conditional. The format for these NON-conditional alleles is:

Gene-symbol$^{tm\#e(project\ abbreviation)Labcode}$

The allele symbol has a superscripted portion comprised of:

tm#e	tm for targeted mutation, followed by a serial number and an ‘e’ indicating an allele of the ‘knockout first, NON-conditional’ type
(project)	enclosed in parentheses, the project abbreviation
Labcode	the laboratory code for the institution or investigator creating the allele.

Example: *Plvap*$^{tm1e(EUCOMM)Hmgu}$	plasmalemma vesicle associated protein; targeted mutation 1e, Helmholtz Zentrum Muenchen GmbH

Derivative alleles of two types can be created from this allele as follows:

1. Gene-symbol$^{tm\#e.1(project\ abbreviation)Labcode}$ is created when the original ‘tm1e’ allele undergoes cre-mediated recombination, which removes the neo cassette.

   The allele symbol has a superscripted portion comprised of:

tm#e.1	tm for targeted mutation, followed by a serial number and an ‘e.1’ indicating an allele of the ‘knockout first, reporter-tagged insertion NON-conditional’ type that has undergone cre-excision
(project)	enclosed in parentheses, the project abbreviation
Labcode	the laboratory code for the institution or investigator who created the *original*

allele (not the lab code of the investigator/institution developing the derivative).

Example: *Npc2*$^{tm1e.1(EUCOMM)Wtsi}$ Niemann Pick type C2; targeted mutation 1e.1, Wellcome Trust Sanger Institute

2. Gene-symbol$^{tm\#e.2(project\ abbreviation)Labcode}$ is created when the original 'tm1e' allele undergoes flp-mediated recombination, which removes the LacZ and neo.

   The allele symbol has a superscripted portion comprised of:

tm#e.2	tm for targeted mutation, followed by a serial number and an 'e.2' indicating an allele of the 'knockout first, reporter-tagged insertion NON-conditional' type that has undergone flp-excision, with both LacZ and neo removed
(project)	enclosed in parentheses, the project abbreviation
Labcode	the laboratory code for the institution or investigator who created the *original* allele (not the lab code of the investigator/institution developing the derivative).

   Example: *Npc2*$^{tm1e.2(EUCOMM)Wtsi}$ Niemann Pick type C2; targeted mutation 1e.2, Wellcome Trust Sanger Institute

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5. Targeted Knockout First Alleles with Artificial Introns.

For genes that are very small or contain only a single exon, vector designs to make conditional-ready alleles fail (requires a critical exon). Conditional knockout first alleles for such genes can be made by introducing an artificial intron into which the targeting cassette is imbedded. The 'second' exon (1b) is then used as the critical exon.

The allele symbol has a superscripted portion comprised of:

tm#a or tm#e	tm for targeted mutation, followed by a serial number and an 'a' indicating an allele of the 'knockout first, conditional-ready' type or 'e' indicating a non-conditional knockout allele (same as in section 3 and 4 above)
(project)	enclosed in parentheses, the project abbreviation
Labcode	the laboratory code for the institution or investigator creating the allele.

The nomenclature for these alleles (and their derivatives) is the same as described above for

3. Targeted Knockout First, Reporter-tagged Insertion with Conditional Potential (conditional-ready)
4. Targeted Knockout First, Reporter-tagged Insertion NON-conditional

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6. Targeted cre Knockin Alleles.

The EUCOMMtools project creates targeted, cre knockin alleles that expand the available worldwide cre resources. These alleles follow the same nomenclature as other knockin alleles.

The allele symbol, for the gene into which sequences have been knocked in has a superscripted portion comprised of:

tm#	tm for targeted mutation, followed by a serial number
(project)	enclosed in parentheses, the project abbreviation
Labcode	the laboratory code for the institution or investigator creating the allele.
Example:	*Hprt*$^{tm1(Cbx1\text{-}cre/ERT2)Hmgu}$	A hypothetical targeted knockin at the *Hprt* locus. The knocked in portion contains promoter sequences from *Cbx1* driving cre/ERT2