



## Bibliography on Alternative Methods of Genotyping Mice

Animal Welfare Information Center, National  
Agricultural Library, US Department of Agriculture,  
<https://www.nal.usda.gov/programs/awic>

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### What is Genotyping?

In the biomedical research field, researchers breed strains of genetically-modified animals (particularly mice) to model human disease. Genetically-modified (GM) mice are created from introducing or editing genes in their DNA. They are bred with wild-type mice to produce lines of offspring carrying the mutated genes.<sup>1</sup> Researchers have also been breeding lines of transgenic rats since 1990.<sup>2</sup>

Rodent colony managers must verify that animals produced in GM breeding programs *actually* carry the specified disrupted gene or transgene. They perform this verification through a process called genotyping, where a tissue sample is taken for DNA analysis. Traditionally, when using weanling mice, researchers obtain DNA by amputating no more than 5 mm of the tail. However, this amputation severs nerves, bones, and skin, which can be problematic if multiple samples need to be taken.<sup>3</sup> In addition, tail amputations or biopsies can cause pain and distress to the animal.<sup>4</sup>

### Less Invasive Alternatives to Genotyping

Tail tip amputation is not the only way to obtain DNA for genotyping rodents. Several less-invasive or non-invasive methods exist, including sampling hair follicles, buccal (mouth) swabs, rectal swabs,<sup>5</sup> and fecal pellets.<sup>6</sup> Discovering less invasive methods of genotyping is considered a refinement method (i.e., a husbandry practice that enhances animal welfare) and thus, furthers the objective of promoting the Three Rs.

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<sup>1</sup> Parker-Thornburg, J. (2020). Breeding Strategies for Genetically Modified Mice. In: Larson, M. (eds) *Transgenic Mouse*. Methods in Molecular Biology, vol 2066. Humana, New York, NY. [https://doi.org/10.1007/978-1-4939-9837-1\\_14](https://doi.org/10.1007/978-1-4939-9837-1_14)

<sup>2</sup> Cozzi, J., Fraichard, A., & Thiam, K. (2008). Use of genetically modified rat models for translational medicine. *Drug discovery today*, 13(11-12), 488–494. <https://doi.org/10.1016/j.drudis.2008.03.021>

<sup>3</sup> Cinelli, P., Rettich, A., Seifert, B., Bürki, K., & Arras, M. (2007). Comparative analysis and physiological impact of different tissue biopsy methodologies used for the genotyping of laboratory mice. *Laboratory Animals*, 41(2), 174–184. <https://doi.org/10.1258/002367707780378113>

<sup>4</sup> Hamann, M., Lange, N., Kuschka, J., & Richter, A. (2010). Non-invasive genotyping of transgenic mice: Comparison of different commercial kits and required amounts. *ALTEX*, 27(3), 185–190. <https://doi.org/10.14573/altex.2010.3.185>.

<sup>5</sup> Cinelli et al, 2007.

<sup>6</sup> Hamann et al, 2010.

## Bibliography

We have included citations on alternative methods of genotyping mice. The bibliography covers articles published from 2000 to 2024.

The following databases were searched:

- PubMed
- Embase
- Web of Science (All databases: Web of Science Core Collection and Biological Abstracts, BIOSIS Science Citation Index, Current Contents Concept, KCI-Korean Journal Database, Russian Science Citation Index, SciELO Citation Index, and Zoological Record)
- EBSCO (Agricola, CAB Abstracts, eBook Collection (EBSCOhost), Environment Complete, Global Health, Zoological Record, Biological Abstracts)

The citations are arranged in alphabetical order by the last name of the first author. We have omitted abstracts due to publisher copyright considerations. The search strategies that we used in these searches are provided following the citations.

These citations discuss genotyping techniques using potentially less-invasive methods than tail biopsy. Recently published studies suggest that rectal (Kaye et al, 2024) or buccal (Lui et al, 2024) swabs are as effective for genotyping rodents because more-invasive sampling involves tissue removal from the tail or ear. Other citations (such as Picazo et al, 2015) discuss the quality of DNA obtained from different sampling sites or from tissues/fluids or from mice of different ages. Silverman & Hendricks (2015) describe neural development in mouse tails and the implications for deciding at what age to perform a biopsy.

We have also included a section called [Web Resources](#) which includes links to websites and other bibliographies on alternative methods of genotyping.

## Finding Abstracts and Full-Text of Articles

We have omitted abstracts due to publisher copyright considerations. However, you can locate abstracts easily by clicking on the DOI (digital object identifier) in the citation. The DOI is a permanent identifier that links to the journal article's page on the journal's website.

There are multiple ways of locating full-text of articles and books in the bibliography. You can check the National Agricultural Library's (NAL) online catalog, [SEARCH](#), to see which books and periodicals the library has in its holdings. Some online periodicals in NAL's holdings are only available to USDA employees through the [Digitop](#) portal. Other articles are open access and may be downloaded for free. If you are not a USDA employee, check with your local or institutional library to see whether your library subscribes to these periodicals or can order them on interlibrary loan.

Information on how to request materials that are included in the National Agricultural Library (NAL)’s collections can be found on the [Request Library Materials](#) page. USDA employees can request books and articles through Document Delivery. All patrons are encouraged to explore local library resources first before contacting the National Agricultural Library. If you are not a USDA employee, you may visit the library during its hours of operation to request items or read electronic articles on-site. You may also request items on interlibrary loan through your home library (check with your institutional, university, or public library’s loan office for further information).

### Related Content: Alternatives to Genotyping Hedges

AWIC has also published Search Hedges for Alternative Methods of Genotyping Rodents which is posted in the [Search Hedges](#) section of AWIC’s Literature Searching web page. A **search hedge** is a prepared search string that can be pasted into a database search interface to find citations on a particular topic or population. We have formatted versions of the Alternatives to Genotyping Hedge for PubMed, Web of Science, Embase, EBSCO and Scopus. These hedges retrieve literature on alternative methods of genotyping rodents (rats and mice). Users can conduct their own searches using the hedges or set up search alerts in bibliographic databases (see “Setting up Search Alerts” on AWIC's Literature Searching/[Additional Resources](#) web page).

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## Citations on Noninvasive Methods of Genotyping in Mice

### Citations:

#### 33 citations

Bonaparte, D., Cinelli, P., Douni, E., Hérault, Y., Maas, M., Pakarinen, P., Poutanen, M., Lafuente, M. S., & Scavizzi, F. (2013). FELASA guidelines for the refinement of methods for genotyping genetically-modified rodents: A report of the Federation of European Laboratory Animal Science Associations Working Group. *Laboratory Animals*, 47(3), 134–145.

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## Strategy:

### PubMed

1. (Mice[MeSH Major Topic] OR mouse[Title/Abstract] OR mice[Title/Abstract] OR mus[Title/Abstract] OR murine[Title/Abstract] OR rodent\*[Title/Abstract]) AND ("Genotyping Techniques"[Mesh Major Topic] OR genotyping[Title] OR (genotyping[Title] AND (Technique\*[Title] OR method\*[Title])) OR (DNA[Title] AND (sampl\*[Title] OR collect\*[Title]))) AND (Animal Use Alternatives[MeSH Terms] OR "Animal Welfare"[Mesh] OR noninvasive[Title/Abstract] OR non-invasive[Title/Abstract] OR "minimally invasive"[Title/Abstract] OR "less invasive"[Title/Abstract] OR less-aversive[Title/Abstract] OR non-aversive[Title/Abstract] OR welfare[Title/Abstract] OR "well-being"[Title/Abstract] OR stress\*[Title/Abstract] OR refine\*[Title/Abstract] OR distress\*[Title/Abstract] OR 3Rs[Title/Abstract] OR "three rs"[Title/Abstract] OR "animal use alternative\*" [Title/Abstract] OR alternative\*[Title/Abstract] OR humane[Title/Abstract] OR "stress-free"[Title/Abstract] OR "low stress"[Title/Abstract] OR "reduce stress"[Title/Abstract] OR pain\*[Title/Abstract] OR anxiety[Title/Abstract] OR "best method\*" [Title/Abstract] OR "best practice\*" [Title/Abstract] OR "preferred method\*" [Title/Abstract] OR recommend\*[Title/Abstract] OR guideline\*[Title/Abstract]) AND ("2000"[Date - Publication] : "2023"[Date - Publication])
2. (Mice[MeSH Major Topic] OR mouse[Title/Abstract] OR mice[Title/Abstract] OR mus[Title/Abstract] OR murine[Title/Abstract] OR rodent\*[Title/Abstract]) AND ("Genotyping Techniques"[Mesh Major Topic] OR genotyping[Title] OR (genotyping[Title] AND (Technique\*[Title] OR method\*[Title])) OR (DNA[Title] AND (sampl\*[Title] OR collect\*[Title]))) AND (Animal Use Alternatives[MeSH Terms] OR "Animal Welfare"[Mesh] OR noninvasive[Title/Abstract] OR non-invasive[Title/Abstract] OR "minimally invasive"[Title/Abstract] OR "less invasive"[Title/Abstract] OR less-aversive[Title/Abstract] OR non-aversive[Title/Abstract] OR welfare[Title/Abstract] OR "well-being"[Title/Abstract] OR

stress\*[Title/Abstract] OR refine\*[Title/Abstract] OR distress\*[Title/Abstract] OR 3Rs[Title/Abstract] OR "three rs"[Title/Abstract] OR "animal use alternative\*" [Title/Abstract] OR alternative\*[Title/Abstract] OR humane[Title/Abstract] OR "stress-free"[Title/Abstract] OR "low stress"[Title/Abstract] OR "reduce stress"[Title/Abstract] OR pain\*[Title/Abstract] OR anxiety[Title/Abstract] OR "best method\*" [Title/Abstract] OR "best practice\*" [Title/Abstract] OR "preferred method\*" [Title/Abstract] OR recommend\*[Title/Abstract] OR guideline\*[Title/Abstract]) AND ("2023"[Date - Publication] : "2024"[Date - Publication])

## Embase

1. (Mouse/exp/mj OR (mouse OR mice OR mus OR murine OR rodent\*):ab,ti) AND (Genotyping/exp/mj OR (genotyping OR (genotyping AND (technique\* OR method\*)) OR (DNA AND (sampl\* OR collect\*)):ti) AND (animal welfare/exp OR (noninvasive OR non-invasive OR "minimally invasive" OR "less invasive" OR less-aversive OR non-aversive OR welfare OR "well-being" OR stress\* OR refine\* OR distress\* OR 3Rs OR "three rs" OR "animal use alternative\*" OR alternative\* OR humane OR "stress-free" OR "low stress" OR "reduce stress" OR pain\* OR anxiety OR "best method\*" OR "best practice\*" OR "preferred method\*" OR recommend\* OR guideline\*):ab,ti) AND [2000-2023]/py
2. (Mouse/exp/mj OR (mouse OR mice OR mus OR murine OR rodent\*):ab,ti) AND (Genotyping/exp/mj OR (genotyping OR (genotyping AND (technique\* OR method\*)) OR (DNA AND (sampl\* OR collect\*)):ti) AND (animal welfare/exp OR (noninvasive OR non-invasive OR "minimally invasive" OR "less invasive" OR less-aversive OR non-aversive OR welfare OR "well-being" OR stress\* OR refine\* OR distress\* OR 3Rs OR "three rs" OR "animal use alternative\*" OR alternative\* OR humane OR "stress-free" OR "low stress" OR "reduce stress" OR pain\* OR anxiety OR "best method\*" OR "best practice\*" OR "preferred method\*" OR recommend\* OR guideline\*):ab,ti) AND [2023-2024]/py

## Web of Science

1. (TI=(mouse OR mice OR mus OR murine OR rodent\*) OR AB=(mouse OR mice OR mus OR murine OR rodent\*)) AND (TI=(genotyping OR (genotyping AND (technique\* OR method\*)) OR (DNA AND (sampl\* OR collect\*)))) AND (TI=(noninvasive OR non-invasive OR "minimally invasive" OR "less invasive" OR less-aversive OR non-aversive OR welfare OR "well-being" OR stress\* OR refine\* OR distress\* OR 3Rs OR "three rs" OR "animal use alternative\*" OR alternative\* OR humane OR "stress-free" OR "low stress" OR "reduce stress" OR pain\* OR anxiety OR "best method\*" OR "best practice\*" OR "preferred method\*" OR recommend\* OR guideline\*)) OR AB=(noninvasive OR non-invasive OR "minimally invasive" OR "less invasive" OR less-aversive OR non-aversive OR welfare OR "well-being" OR stress\* OR refine\* OR distress\* OR 3Rs OR "three rs" OR "animal use alternative\*" OR alternative\* OR humane OR "stress-free" OR "low stress" OR "reduce stress" OR pain\* OR anxiety OR "best method\*" OR "best practice\*" OR "preferred method\*" OR recommend\* OR guideline\*)) AND (PY=(2000-2023))



2. (TI=(mouse OR mice OR mus OR murine OR rodent\*) OR AB=(mouse OR mice OR mus OR murine OR rodent\*)) AND (TI=(genotyping OR (genotyping AND (technique\* OR method\*)) OR (DNA AND (sampl\* OR collect\*)))) AND (TI=(noninvasive OR non-invasive OR "minimally invasive" OR "less invasive" OR less-aversive OR non-aversive OR welfare OR "well-being" OR stress\* OR refine\* OR distress\* OR 3Rs OR "three rs" OR "animal use alternative\*" OR alternative\* OR humane OR "stress-free" OR "low stress" OR "reduce stress" OR pain\* OR anxiety OR "best method\*" OR "best practice\*" OR "preferred method\*" OR recommend\* OR guideline\*) OR AB=(noninvasive OR non-invasive OR "minimally invasive" OR "less invasive" OR less-aversive OR non-aversive OR welfare OR "well-being" OR stress\* OR refine\* OR distress\* OR 3Rs OR "three rs" OR "animal use alternative\*" OR alternative\* OR humane OR "stress-free" OR "low stress" OR "reduce stress" OR pain\* OR anxiety OR "best method\*" OR "best practice\*" OR "preferred method\*" OR recommend\* OR guideline\*)) AND (PY=(2023-2024))

**EBSCO (Biological Abstracts, Agricola, CAB Abstracts, eBook Collection (EBSCOhost), Global Health, Zoological Record)**

1. (TI (mouse OR mice OR mus OR murine OR rodent\*) OR AB (mouse OR mice OR mus OR murine OR rodent\*)) AND (TI (genotyping OR (genotyping AND (technique\* OR method\*)) OR (DNA AND (sampl\* OR collect\*)))) AND (TI (noninvasive OR non-invasive OR "minimally invasive" OR "less invasive" OR less-aversive OR non-aversive OR welfare OR "well-being" OR stress\* OR refine\* OR distress\* OR 3Rs OR "three rs" OR "animal use alternative\*" OR alternative\* OR humane OR "stress-free" OR "low stress" OR "reduce stress" OR pain\* OR anxiety OR "best method\*" OR "best practice\*" OR "preferred method\*" OR recommend\* OR guideline\*)) OR AB (noninvasive OR non-invasive OR "minimally invasive" OR "less invasive" OR less-aversive OR non-aversive OR welfare OR "well-being" OR stress\* OR refine\* OR distress\* OR 3Rs OR "three rs" OR "animal use alternative\*" OR alternative\* OR humane OR "stress-free" OR "low stress" OR "reduce stress" OR pain\* OR anxiety OR "best method\*" OR "best practice\*" OR "preferred method\*" OR recommend\* OR guideline\*))

Limiters: Date Published 2000-2023

2. (TI(mouse OR mice OR mus OR murine OR rodent\*) OR AB(mouse OR mice OR mus OR murine OR rodent\*)) AND (TI(genotyping OR (genotyping AND (technique\* OR method\*)) OR (DNA AND (sampl\* OR collect\*)))) AND (TI(noninvasive OR non-invasive OR "minimally invasive" OR "less invasive" OR less-aversive OR non-aversive OR welfare OR "well-being" OR stress\* OR refine\* OR distress\* OR 3Rs OR "three rs" OR "animal use alternative\*" OR alternative\* OR humane OR "stress-free" OR "low stress" OR "reduce stress" OR pain\* OR anxiety OR "best method\*" OR "best practice\*" OR "preferred method\*" OR recommend\* OR guideline\*)) OR AB(noninvasive OR non-invasive OR "minimally invasive" OR "less invasive" OR less-aversive OR non-aversive OR welfare OR "well-being" OR stress\* OR refine\* OR distress\* OR 3Rs OR "three rs" OR "animal use alternative\*" OR alternative\* OR humane OR "stress-free" OR "low stress" OR "reduce stress" OR pain\* OR anxiety OR "best method\*" OR "best practice\*" OR "preferred method\*" OR recommend\* OR guideline\*))

Limiters - Publication Date: 20230101-20241231

Expanders - Apply equivalent subjects

Search modes - Terms searched within 5 words

## Web Resources on Alternative Methods of Genotyping

1. Genotyping, A Noninvasive Way of Genotyping Your Mouse Colonies:  
<https://www.criver.com/eureka/noninvasive-way-genotyping-your-mouse-colonies>
2. Animal Welfare Institute, <https://awionline.org/taxonomy/term/378>  
Bibliography of citations on noninvasive methods of genotyping animals.
3. Methods of Collecting Genetic Material for Genotyping, Guidelines for Acceptable Methods of Identification and Genotyping of Rodents and Zebrafish, Institutional Animal Care & Use Committee, University of Michigan,  
<https://az.research.umich.edu/animalcare/guidelines/guidelines-acceptable-methods-identification-and-genotyping-rodents-and>  
Lists procedures for both noninvasive and invasive methods of genotyping.