



Search Hedges for Alternative Methods of Genotyping Rodents

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

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Introduction

The National Agricultural Library's [Animal Welfare Information Center](#) (AWIC) conducts annual workshops for scientists, Institutional Animal Care and Use Committee (IACUC) members, students, librarians, veterinarians, animal care personnel, and others constructing a "Three Rs" literature search.

Over the past few decades, members of the research community have made great strides in finding ways to address the Three Rs and have written a great body of literature on the topic. Despite this, scientists and researchers often cite the difficulty of finding Three Rs citations in bibliographic databases. Researchers commonly report in their animal use protocols that they did not find any Three Rs literature on their topic, yet their search terms consisted mainly of "refinement," "reduction," "replacement," "Three Rs," and "alternatives." We've found that people who use *only* these terms do not find a lot of relevant results.

One of the reasons why Three Rs articles are hard to locate is that authors may not include words such as "Three Rs," "alternatives," "refinement," etc., in abstracts or keywords, even though they may discuss Three Rs concepts or practices in the body of their papers.

Search hedges and search filters are constructed search strings used to find citations on a particular populations, diseases, or publication type. We have created search hedges for various Three Rs concepts (such as environmental enrichment, noninvasive blood sampling methods, etc.) to help scientists, researchers, and librarians locate citations on alternatives.

What is a Search Hedge?

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. Hedges are used frequently in biomedical literature searches to find literature on diseases or populations. They include synonyms or variants of terms. Hedges can save searchers time because the relevant keywords have already been selected for them. Searchers can also combine hedges with the Boolean AND to find a subset of citations on a particular topic. For example, you could combine an environmental enrichment hedge with a species hedge for mice. AWIC has been working on developing hedges on Three Rs topics to facilitate searching for literature on animal use alternatives.

While hedges can help retrieve relevant citations on a particular topic, they are never 100% effective. Searchers will need to review results carefully and recognize that there may be other pertinent articles not retrieved by the hedge.

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.¹ Researchers have also been breeding lines of transgenic rats since 1990.²

The managers of rodent colonies 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.³ In addition, tail amputations or biopsies may cause pain and distress to the animals.⁴

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,⁵ and fecal pellets.⁶ 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.

Hedges

Due to the complex syntax and the choice to search certain database fields, we have provided the full search syntax for this search hedge for PubMed, Web of Science, Scopus, EBSCO, Embase, and for other databases.

¹ 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

² 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>

³ 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>

⁴ 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>.

⁵ Cinelli et al, 2007.

⁶ Hamann et al, 2010.

Please note that although we have made our best efforts to create a search hedge that will retrieve citations on less-invasive methods for genotyping rodents, not every citation in the results will be relevant. We recommend browsing through at least the first 50 results for each hedge (although relevant results may be found further down the results list). We also suggest that you set the database's results display order to "Best Match" or "Relevance" (most databases sort by relevance by default).

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PubMed

("Mice"[MeSH Major Topic] OR "Rats"[MeSH Major Topic] OR "Rodentia"[MeSH Major Topic] OR mouse[Title/Abstract] OR mice[Title/Abstract] OR mus[Title/Abstract] OR murine[Title/Abstract] OR rat[Title/Abstract] OR rats[Title/Abstract] OR rattus[Title/Abstract] OR R-norvegicus[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 Terms] 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 wellbeing[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 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])

Scopus

(TITLE(mouse OR mice OR mus OR murine OR rodent* OR rat OR rats OR rattus OR R-norvegicus) OR ABS(mouse OR mice OR mus OR murine OR rodent* OR rat OR rats OR rattus OR R-norvegicus)) AND (TITLE(genotyping OR (genotyping AND (technique* OR method*)) OR (DNA AND (sampl* OR collect*)))) AND (TITLE(noninvasive OR non-invasive OR minimally-invasive OR less-invasive OR less-aversive OR non-aversive OR welfare OR well-being OR wellbeing OR stress* OR refine* OR distress* OR 3Rs OR three-rs OR animal-use-alternative* OR alternative* OR humane OR pain* OR anxiety OR best-method* OR best-practice* OR preferred-method* OR recommend* OR guideline*) OR ABS(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 pain* OR anxiety OR best-method* OR best-practice* OR preferred-method* OR recommend* OR guideline*))

Web of Science

(TI=(mouse OR mice OR mus OR murine OR rodent* OR rat OR rats OR rattus OR R-norvegicus) OR AB=(mouse OR mice OR mus OR murine OR rodent* OR rat OR rats OR rattus OR R-norvegicus)) 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 wellbeing OR stress* OR refine* OR distress* OR 3Rs OR three-rs OR animal-use-alternative* OR alternative* OR humane 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 pain* OR anxiety OR best-method* OR best-practice* OR preferred-method* OR recommend* OR guideline*))

EBSCO

(TI(mouse OR mice OR mus OR murine OR rodent* OR rat OR rats OR rattus OR R-norvegicus) OR AB(mouse OR mice OR mus OR murine OR rodent* OR rat OR rats OR rattus OR R-norvegicus)) 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 wellbeing OR stress* OR refine* OR distress* OR 3Rs OR three-rs OR animal-use-alternative* OR alternative* OR humane 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 pain* OR anxiety OR best-method* OR best-practice* OR preferred-method* OR recommend* OR guideline*))

Embase

('Mouse'/exp/mj OR 'Rat'/exp/mj OR 'rodent'/exp/mj OR (mouse OR mice OR mus OR murine OR rodent* OR rat OR rats OR rattus OR r-norvegicus):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 pain* OR anxiety OR best-method* OR best-practice* OR preferred-method* OR recommend* OR guideline*):ab,ti)

Other Databases

(mouse OR mice OR mus OR murine OR rodent* OR rat OR rats OR rattus OR r-norvegicus) AND (genotyping OR ((collect* OR sampl*) AND DNA)) AND (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*)

How to Use These Hedges

Below are instructions on how to use these hedges in a few selected databases.

PubMed

1. Select and copy the hedge.
2. Go to <https://pubmed.ncbi.nlm.nih.gov/> and select Advanced to access the Advanced Search Builder
3. Paste the hedge into the Query Box and select Search.
4. You will see the results listed by title and sorted by relevance ("Best Match"). Usually the most relevant citations (the ones that contain multiple keywords from the hedge) appear at the top of the results while less relevant citations tend to be towards the end. Make sure to screen the whole record, because sometimes the refinement is discussed in the abstract and not the title.

Scopus

1. Scopus is a subscription database produced by Elsevier which also publishes peer-reviewed journals and books. You will need to access Scopus through your library's website. Keep in mind that not all institutional libraries subscribe to Scopus. Check with your institution's librarian for advice on how to access Scopus on your library's platform.
2. Go to Scopus' main search page and follow the link for the Advanced Document Search option.
3. Copy and paste the search hedge into the Advanced search query box where it says "Enter query string" and select Search. Scopus will then display the results.
4. By default, Scopus sorts results by default to show the highest cited articles first. Switch the sort order to Relevance so that the most on-target citations display first.

Web of Science

1. Web of Science is a subscription database produced by Clarivate Analytics. You will need to access Web of Science through your library's website. Keep in mind that not all institutional libraries subscribe to Web of Science. Check with your institution's librarian for advice on how to access Web of Science on your library's platform.

2. Go to Web of Science's search page and select the Advanced Search option below the query box.
3. Copy the search hedge and paste it into the Advanced Search Query Builder. Then select the purple Search button.
4. Search results will be displayed sorted by Relevance.

Embase

Embase is the largest subscription biomedical database, produced by Elsevier. It also searches Medline and has its own controlled vocabulary, Emtree, which is based on MeSH.

Copy the search hedge and paste it into Embase's Quick Search dialog box and select the Show Results button. The Search History and a list of results will appear on the next screen.

For additional help

1. You can also translate search strings using [Polyglot](#), a free online tool from Bond University's Institute for Evidence-Based Healthcare.
2. For more information on conducting searches in PubMed, please refer to the Network of the National Library of Medicine's [How PubMed Works](#) instructional video series and [PubMed's User Guide](#).
3. For additional information on search best practices, search syntax, and related topics, see the [Literature Searching: How to Find Animal Use Alternatives](#), on the National Agricultural Library's (USDA) website.
4. If you have questions or suggestions, please reach out to AWIC at awic@usda.gov.