Best Practices for Conducting a Search for Alternatives and Finding Animal Model/Model Organism Information

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LITERATURE SEARCHING FOR ANIMAL USE ALTERNATIVES

December 9, 2021

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USDA, National Agricultural Library (NAL), Animal Welfare Information Center (AWIC)





OBJECTIVES

- Brief Overview of the Animal Welfare Act
- 3Rs Alternatives
- Alternatives Literature Search Demonstration
- AWIC Products and Services





Food Security Act of 1985

Subtitle F, Animal Welfare, Public Law 99-198
Improved Standards for Laboratory Animals Act
https://awahistory.nal.usda.gov/search/5238128

"...the farm bill contains legislation dealing with the humane treatment of animals. The main thrust of the bill is to minimize pain and distress suffered by animals used for experiments and tests. In so doing, biomedical research will gain in accuracy and humanity. We owe much to laboratory animals and that debt can best be repaid by good treatment and keeping painful experiments to a minimum."



AWA Defines Service at NAL

(7 U.S.C. 2142, Sec. 13, Subsection e)

The Secretary shall establish an information service at the National Agricultural Library. Such service shall, in cooperation with the National Library of Medicine, provide information—

- 1. pertinent to employee training;
- which could prevent unintended duplication of animal experimentation as determined by the needs of the research facility; and
- 3. on improved methods of animal experimentation which could--
 - (a) reduce or replace animal use; and
 - (b) minimize pain and distress to animals, such as anesthetic and analgesic procedures.



3Rs Alternatives





History of the 3Rs

"The 3Rs, as first described... by Russell and Burch in 1959 in their book "Principles of Humane Experimental Technique", are regarded as new scientific methods that incorporate some aspect of replacement, reduction, or refinement of animal use in pursuit of the minimization of animal pain and distress consistent with the goals of the research."

https://caat.jhsph.edu/principles/the-principles-of-humane-experimental-technique









Replacement

Substituting sentient animals with insentient material

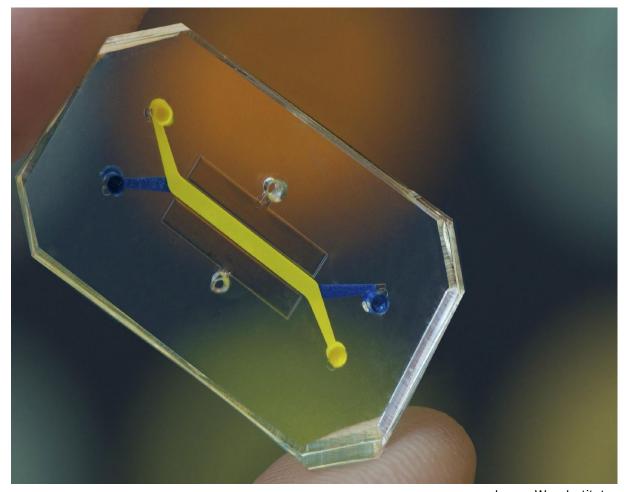


Image: Wyss Institute

Traditional Method: Sentinel Animals

"The colony's soiled bedding is collected and placed in the *sentinel animal's cage to see if the animal becomes infected with a bacteria, virus, or parasite."

-LARC



^{*}Animals used as a monitoring tool to observe animal groups for infectious agents that may impact the health of the animals as well as the experimental study.



Replacement Method: Environmental Health Monitoring

Methods such as exhaust air dust testing and PCR testing of filter material or swabs can replace sentinel animals to detect specific pathogens



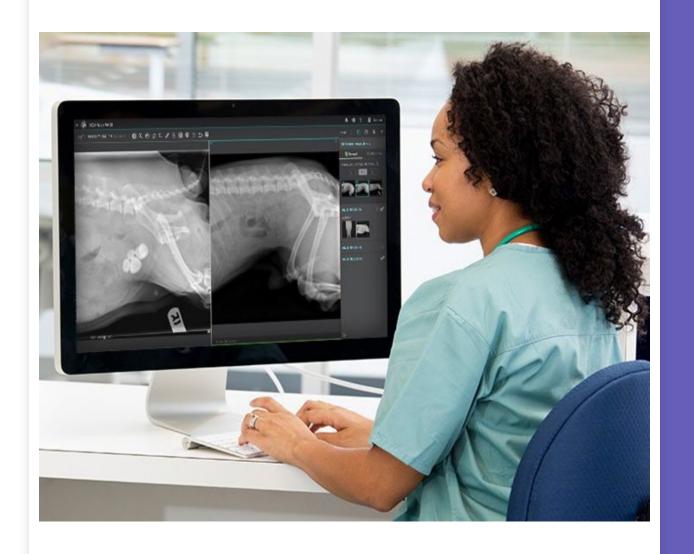






Reduction

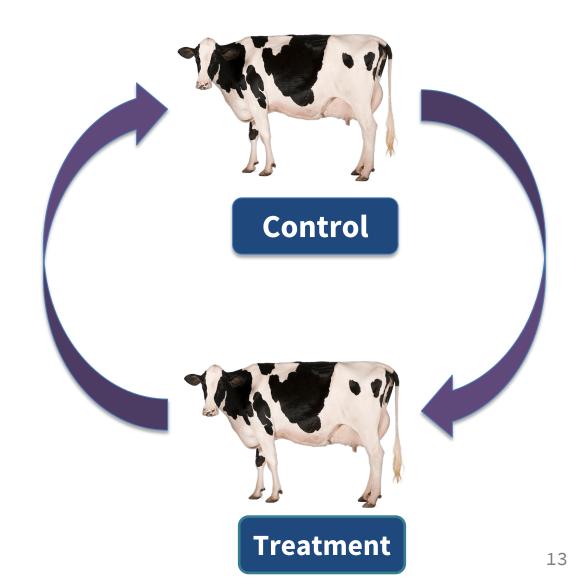
Reduction in the number of animals required per experiment/study while still achieving robust results





Animals Serving as Their Own Control

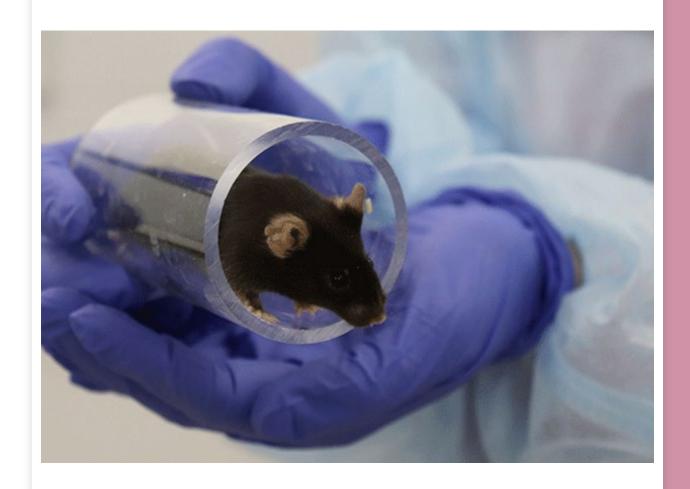
- Same animal experiencing control and treatment groups = fewer animals
- Reduces variability in results!
- Example:
 - Tracked cow A's steps for 24 hours (control)
 - Tracked cow A's steps during 24hour laying- deprivation period (treatment)





Refinement

Methods that minimize animal suffering and improve animal welfare





Handling & Training

Remember: less is more

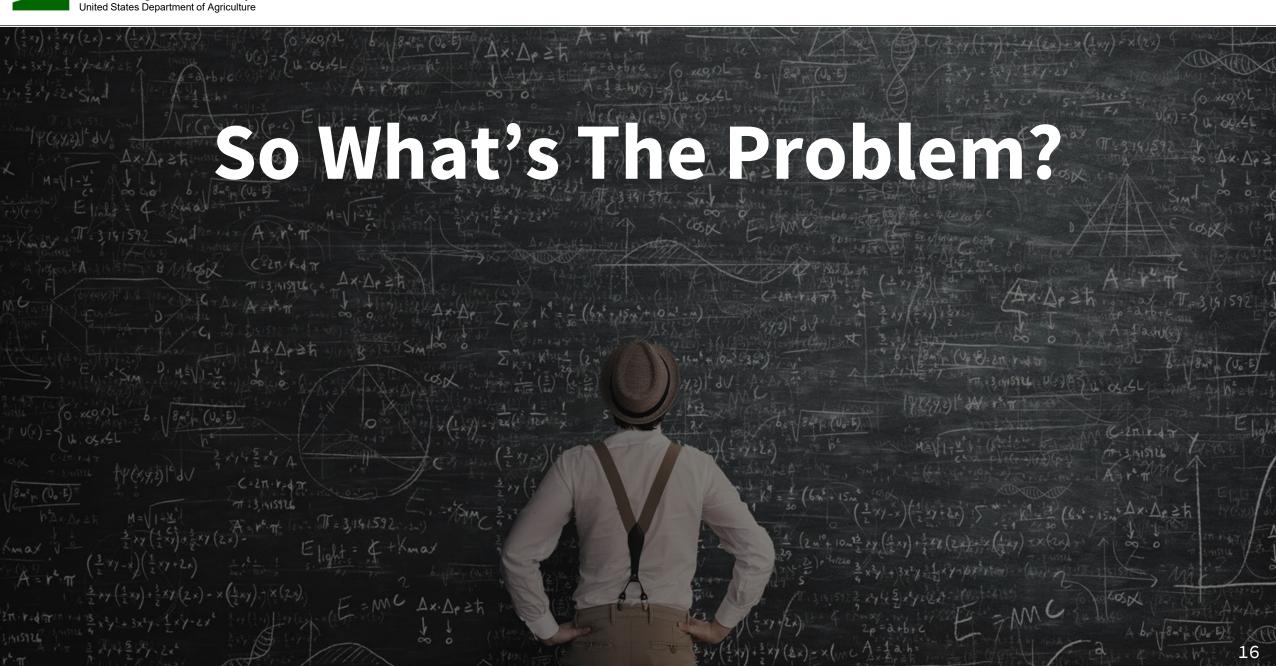


Rat Tickling
https://www.youtube.com/watch?v=78PfGQbL-g0









Decreased Discoverability of 3Rs Citations



"...This is the first study to demonstrate that pair housing improves the affective aspect of calf welfare when compared to individual housing."

Bučková, K., Špinka, M. & Hintze, S. Pair housing makes calves more optimistic. *Sci*

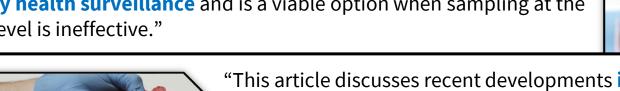
"...These results suggest that nesting material enrichment provided throughout an animal's life may reduce overgrooming-related self-injury."

Khon SV Corroia V Ilhria A Nostina material enrichment reduces severity of overgrooming-related self

"...These findings suggest that **testing media in pooled soiled bedding samples is more effective than traditional sentinel methods for colony health surveillance** and is a viable option when sampling at the rack level is ineffective."

Need Help Searching Literature?

Contact AWC!



Hanso Metho *Scien*o

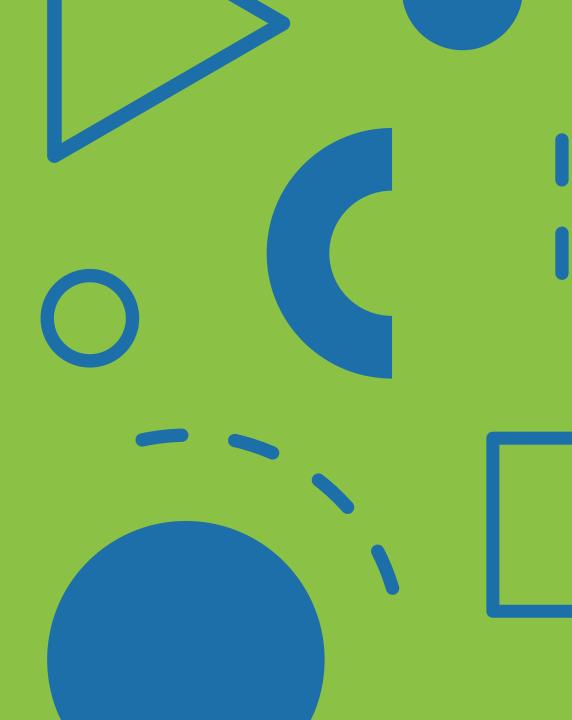


"This article discusses recent developments in soft-tissue surgery teaching...A silion-based, life-like canine ovariohysterectomy model was developed with the assistance of a model-making and special effects company."

Gopinath D, McGreevy PD, Zuber RM, Klupiec C, Baguley J, Barrs VR. Developments in undergraduate teaching of small-animal soft-tissue surgical skills at the University of Sydney. J Vet Med Educ. 2012 Spring;39(1):21-9. doi: 10.3138/jvme.0411.044R. PMID: 22430078.

Conducting a Literature Search

SEARCH DEMONSTRATION





Search Example: Housing of Mice

A research lab is planning multiple studies using a strain of common laboratory white mice. They are planning to house the mice in stacked wire cages with feeders/waterers. Mice are individually housed in steel cages with no bedding or other enrichments.

What 3Rs modifications could be made to this housing model to improve animal wellbeing and reduce stress?





Example: Identify Key Concepts/Keywords

A research lab is planning multiple studies using a strain of common laboratory white mice. They are planning to house the mice in stacked wire cages with feeders/waterers. Mice are individually housed in steel cages with no bedding or other enrichments.

Concept/Keyword Type	Search Terms/Keyword
Housing	housing
Animal	mice
3Rs Alternative	"environmental enrichment*"

Terminology for Refinement Alternatives

- analgesic or analgesia or pain reduction
- anesthetic or anasthetic or anaesthetic
- animal welfare or well-being or wellness or colony management
- assay or technique or method or procedure
- bedding or substrate
- behavior or behaviour or ethology
- blood draw or blood sampling or sample sites (intravenous, tail vein, saphenous vein, etc.)
- challenge method or infection
- environmental enrichment
- euthanasia or humane endpoint
- grimace scales (for pain monitoring)
- handling or humane handling or humane restraint or humane treatment

- husbandry or housing or caging
- imaging or scanning (MRI, magnetic resonance imagery, PET scans, positron emission tomography, CAT scans, bioluminescent scanning)
- injection or injection site
- non-invasive or less-invasive
- pain or stress or distress
- positive reinforcement training or animal training
- refinement
- social housing or group housing
- telemetry device, monitoring device, biotelemetry

Most search terms are obtained from the protocol and area of study.



Terminology for Reduction Alternatives

- animal model
- animal study registries
- auto control (using animal as its own control)
- biomarker or biological marker
- computational methods, computational models, in silico
- data repositories or reuse data
- experimental or statistical design (pilot study, variation, sample size, etc.)
- imaging or scanning (MRI, magnetic resonance imagery, PET scans, positron emission tomography, CAT scans, bioluminescent scanning)
- Microsampling

- monitoring device or telemetry device, biotelemetry
- pilot study
- reduce or reduction or minimize or "use fewer animals"
- reusing or sharing or repurposing animals (between studies)
- sample size or "number of animals"
- tissue banks
- variation (i.e., minimizing variation among animals in study)



Terminology for Replacement Alternatives

- animal testing alternative or animal use alternative or alternative (useful primarily in toxicology and education)
- cadaver or carcass
- cell culture, cell line
- computer aided instruction, computer assisted instruction
- computational methods or models (in silico)
- computer (simulation or application or model)
- digital imaging
- interactive
- in vitro
- isolated (cell, tissue, organ)
- mannequin or manikin or model (non-animal)
- mathematical (computational biology or model or simulation)

- model (animal, cadaveric, interactive, mathematical, statistical, theoretical), modeling (US spelling or modelling (UK spelling)
- non-animal model
- organ-on-a-Chip or microfluidic device
- organoids or 3-D organoids
- plastinate or plastination
- software
- replacement alternatives
- simulation or simulator or trainer
- structure evaluated system
- tissue culture or organ culture
- tissue engineering
- video (disc, display)
- virtual (reality)



Combining The Search Strings

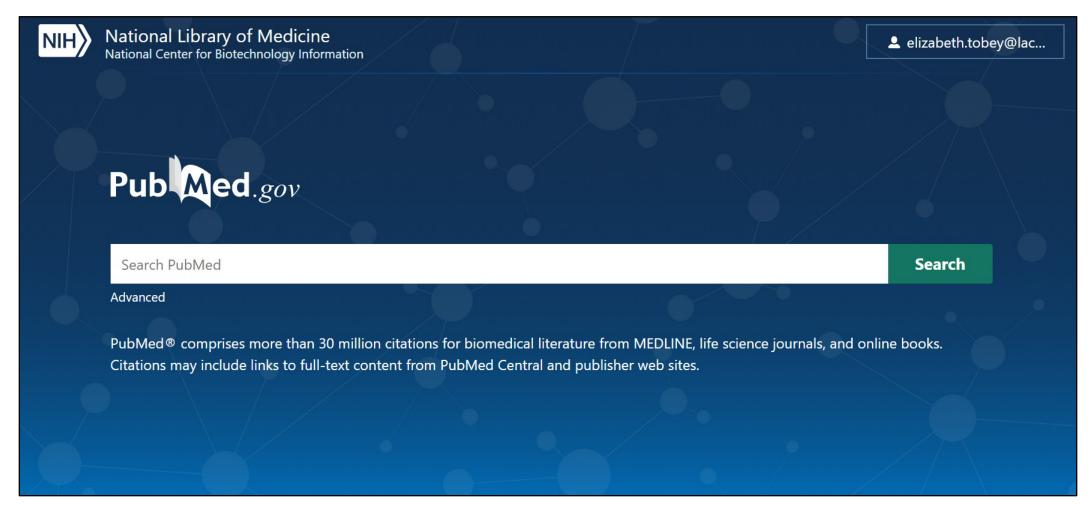
Housing: housing OR cage OR enclosure.

Animal: mice OR mouse OR murine OR mus.

• 3Rs: "environmental enrichment*" OR "social housing" OR toys OR "animal welfare" OR "reduce stress" OR bedding OR "nesting material*".



PubMed



https://pubmed.ncbi.nlm.nih.gov/

Evaluate and Refine the Search Based on Results

- If most of the results are relevant, the search strategy doesn't need another concept added.
- If the results are too broad, consider limits:
 - Publication year.
 - Specific fields (e.g., title, keywords, abstract).
- Fix what you can
 - Add a NOT group of things to exclude.
 - Fix any unintended truncations results.



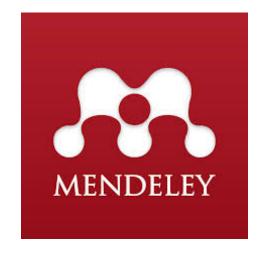
Document Your Search!

Maintain citation lists.

- Endnote
- Refworks
- Mendeley
- Zotero









EndNote



Citation that Incorporates 3Rs Alternatives

André V, Gau C, Scheideler A, Aguilar-Pimentel JA, Amarie OV, Becker L, et al. (2018) Laboratory mouse housing conditions can be improved using common environmental enrichment without compromising data. PLoS Biol 16(4): e2005019. https://doi.org/10.1371/journal.pbio.2005019

From the abstract:...."...nesting material and shelters may be used to improve animal welfare without impairment of experimental outcome or loss of comparability to previous data collected under barren housing conditions."





Search Evaluation Red Flags

Only one database searched.

Terms only for painful aspects.

The term "alternative" used alone with no other 3Rs terms.

Keywords listed not relevant to protocol.

Keywords and concepts linked in an incorrect manner (e.g., wrong Boolean operators).

Search doesn't cover adequate time period (5-10 years).



How many databases do you typically use when conducting a literature search?





Best Databases for Animal Welfare and Alternatives Info

AGRICOLA

PubMed

Web of Science

EMBASE

Scopus

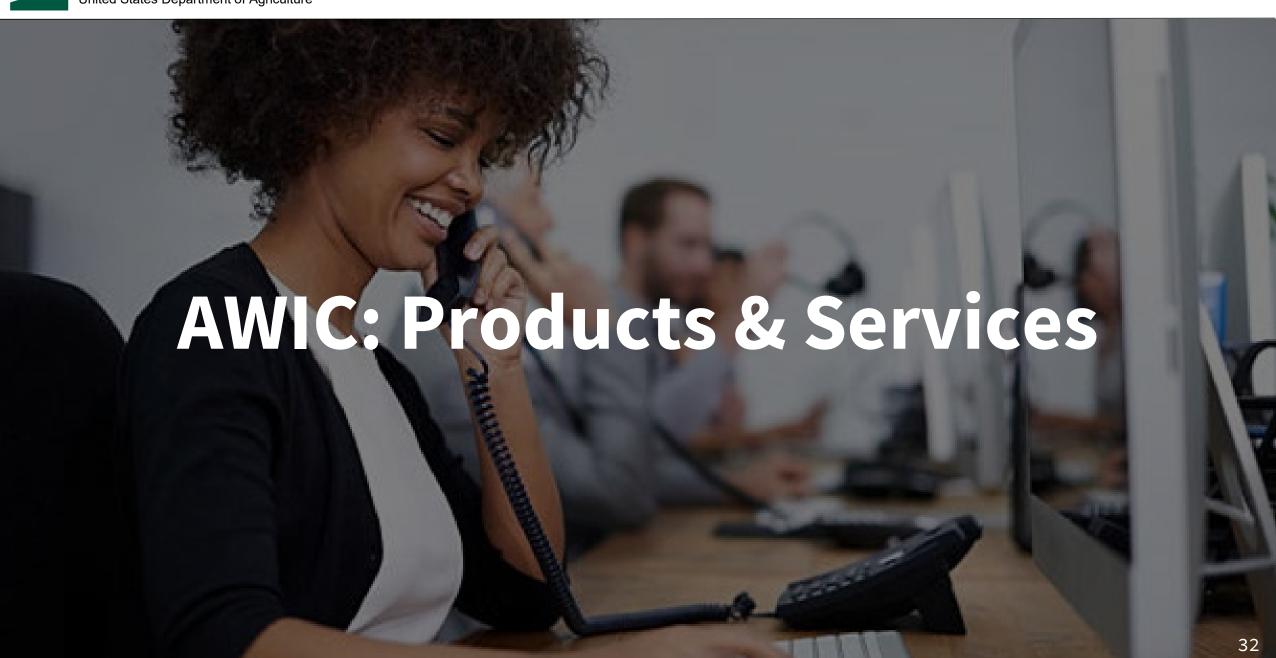
BIOSIS

PsycInfo

CAB Direct

Zoological Record Aquatic
Sciences and
Fisheries
Abstracts







National Agricultural Library Resources



National Agricultural Library (NAL)

https://www.nal.usda.gov/

Animal Welfare Information Center (AWIC)

https://www.nal.usda.gov/legacy/awic





AWIC Workshops

AWIC Workshop & Trainings

require that investigate

Meeting the Requirements of the Animal Welfare Act

This in-person workshop is intended for the regulated community (any personnel working with animals in research, testing, or education) and is typically held at the National Agricultural Library (NAL) in Beltsville, Maryland. However, due to COVID-19, AWIC is offering this workshop through a virtual platform.

About the Workshop

The regulation (IACL) constrati dures the March 9, October May 11, 6, 2021 2022 2022 (virtual) (virtual) (virtual)

-+itutional Animal Care --



- A historical overview of the Animal Welfare Act (AWA), and regulations
- What is meant by the Information requirements of the Animal Welfare Act (AWA).
- 3Rs Alternatives of Reduction, Refinement, and Replacement
- Databases and resources available to access scientific literature
- A systematic approach to accessing information and creating effective literature search strategies.

Access Anytime!

To Register: https://go.usa.gov/xHFRH

To Register: http://bit.ly/2ZLkAtd



Customizable Trainings

Freely provided upon request

Information Requirements of the AWA

History of the Animal Welfare Act

3Rs Alternatives/Resources

Conducting a Literature Search

Animal Welfare Information Center (AWIC)



AWIC assists patrons with searching literature and provides customizable training opportunities.

https://bit.ly/3lofaPe

Need Assistance? Complete a request <u>form!</u>

https://www.nal.usda.gov/legacy/sites/default/files/alt_lit_search_form.pdf



AWIC Helps You PREPARE For Better Science



Featured photo by: Gettylmages

Current concerns about reproducibility in preclinical research make it even more important to plan animal studies properly. Sometimes, finding this high-quality information can be difficult, but AVIVC can help with identifying the right resourcest AWIC provides information on searching published literature and resources that can assist with experimental design.

Among these resources are the <u>PREPARE guidelines</u>, created by <u>Norecopa</u>. The <u>PREPARE</u> guidelines are a two-page checidist, containing essential topics that scientists should consider when planning experiments. These guidelines are useful to those looking for the latest resources on how to conduct better science, optimize animal welfare, and improve the reproducibility and translatability of animal research.

Visit the AWIC website for the latest resources on 3Rs information and technology, or contact us for additional support.

Training and Conferences

Scientists Center for Animal Welfare (SCAW)

December 7, 2020 - December 3, 2020

Meeting the Information Requirements of the Animal Welfare Act

Maroh 24, 2021 - Maroh 26, 2021



Stay plugged in to AWIC updates! SUBSCRIBE



Pets Reduce Animal Use in Research



Certer for Image-Guided Animal Therapy

International Women's Day on March 8th, the Animal Welfare Information Center swomen scientists conducting research into the development and use of 3Rs

ecent experiments at the Johns Hopkins University's Center for Image-Guided use of pets with pre-existing diseases. This method reduces the number of imals required. With the information collected, <u>Dr. Bara Kratishman</u>, VMD, Ph.D. inflored Imaging protectis applicable to both humans and pets. You can watch m Dr. Kratishman and other women scientists who presented their research at the Symposium in June 2020.

out CIGAT and other reduction methods in research, visit AWIC's 7th Annual 3Rs page or contact AWIC.

Training and Conferences

he Information Requirements of the Animal Welfare Act March 26, 2021 (Virtual)



Stay plugged in to AWIC updates! SUBSCRIBE

AWIC Newsletter



New 3Rs research



Literature searching tips



3Rs conferences/trainings



Researchers using 3Rs methods



Contacting AWIC

https://www.nal.usda.gov/awic

Tel (AWIC): (301) 504-6212

E-mail: awic@usda.gov

Animal Welfare Information Center (AWIC) National Agricultural Library 10301 Baltimore Avenue, Room 109 Beltsville, MD 20705





Best Practices for Finding Animal Model/Model Organism Information

Joelle Mornini, MLS Informationist, NIH Library Joelle.Mornini@nih.gov

Objectives



• After completing this training, you will be able to:

- Describe the difference between animal models, research organisms, and model organisms
- Identify requirements for the NIH Model Organism Sharing Policy
- Locate biomedical articles and patents related to animal models
- Locate NIH-funded research projects, genetic information, and biomedical literature related to specific research organisms



Animal Models and Model Organisms





Definitions



Animal Models

- An animal with a disease either the same as or like a disease in humans
- Used to study the development and progression of diseases and to test new treatments before they are given to humans
- Definition source: <u>NCI Dictionary of Cancer Terms</u> (https://bit.ly/3I0VBad)
- Research Organism: Any creature that scientists use to study life
- Model Organism: When research organisms are used to examine elements of human disease
 - Examples: Fruit fly, mouse, rat, zebrafish
 - Definition source: <u>Research Organisms (NIGMS)</u> (https://bit.ly/3xD3VbE)



Relationship of Model Organisms and Animal Models





Model organisms are often used as animal models in the study of human diseases, and terms can often be used interchangeably

Rat (example of a model organism)

"Rat in Research for Animal Testing"
(https://www.flickr.com/photos/90500915@N05/8223128161) by www.understandinganimalres earch.org.uk is licensed under CC BY 2.0

Zebrafish (example of a model organism)

"NIH Zebrafish Facility"

(https://www.flickr.com/photos/132318516@N08/276 79402256) by National Institutes of Health (NIH) is licensed under CC BY-NC 2.0



NIH Model Organism Sharing Policy





NIH Model Organism Sharing Policy Description



NIH Policy on Sharing of Model Organisms for Biomedical Research: Extension of NIH policy on sharing research resources

- Effective October 1, 2004, for applications or proposals to NIH
- Applies to extramural investigators funded by NIH grants, cooperative agreements, and contracts

All NIH applications and proposals that will produce new, genetically modified variants of model organisms expected to include a sharing plan or state why sharing is not possible





NIH Model Organism Sharing Policy Resources



Check NIH Model Organism Information

(https://grants.nih.gov/grants/policy/ model_organism/) for:

- Original NIH Guide Notice
 - NOT-OD-04-042 (https://bit.ly/3loOc4G)
- FAQ on sharing of model organisms
- Example plans (simple plan, complex plan, and plan for sharing mice)



<u>Sharing Policy (PDF)</u>
(https://bit.ly/3pdkve8)



Finding Biomedical Articles on Animal Models





Finding Biomedical Articles: PubMed & MeSH



- PubMed® (https://pubmed.ncbi.nlm.nih.gov/) is a free biomedical literature database from the National Library of Medicine
 - Use controlled vocabulary for PubMed, the Medical Subject Headings (MeSH terms), to search for articles with MeSH "Models, Animal" (https://bit.ly/3o5eGQw)

All MeSH Categories

Analytical, Diagnostic and Therapeutic Techniques and Equipment Category
Investigative Techniques

Models, Animal

Disease Models, Animal

Arthritis, Experimental

Diabetes Mellitus, Experimental

Liver Cirrhosis, Experimental

Neoplasms, Experimental +

Nervous System Autoimmune Disease, Experimental +

Radiation Injuries, Experimental

Isolated Heart Preparation

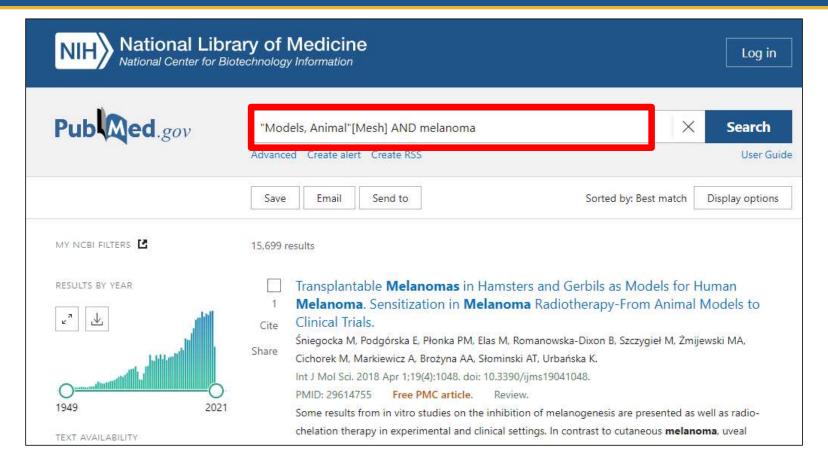
When searching PubMed using MeSH, all narrower MeSH terms under a broader term (like Models, Animal) are also automatically included in the search





Finding Biomedical Articles: PubMed







Finding Patents on Animal Models

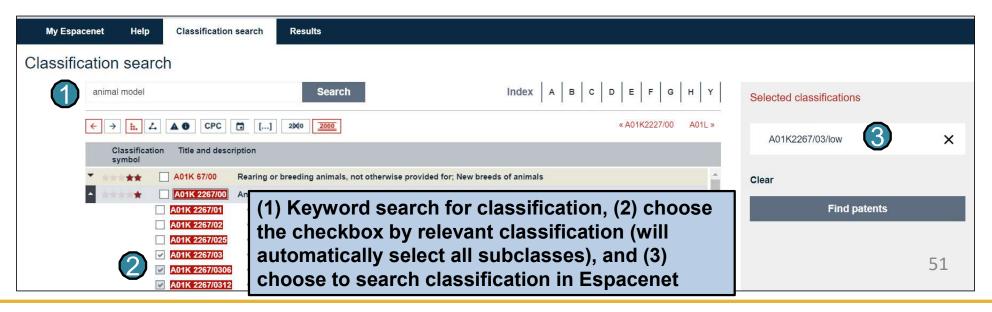




Finding Patents on Espacenet: CPC

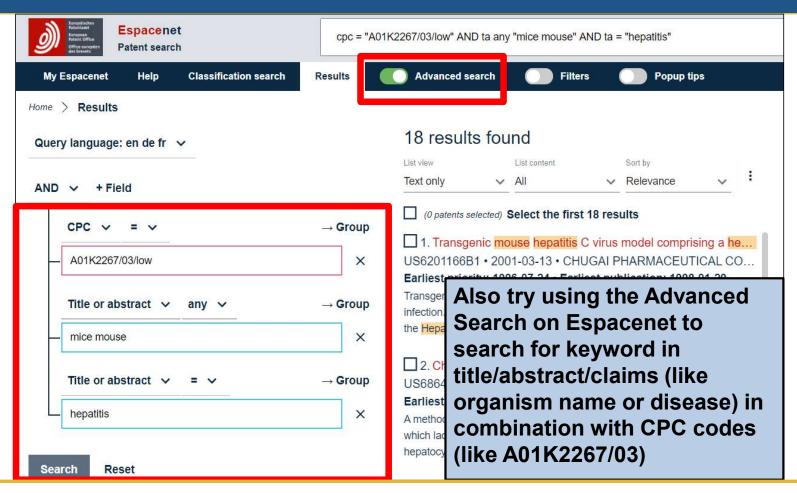


- Espacenet (https://worldwide.espacenet.com/), a free patent search tool from the European Patent Office
- Use the Cooperative Patent Classification (CPC) browser to find classifications related to animal models and model organisms
 - Example: A01K2267/03 (https://bit.ly/3D3sy20) Animal model, e.g. for test or diseases





Finding Patents on Espacenet: Advanced Search





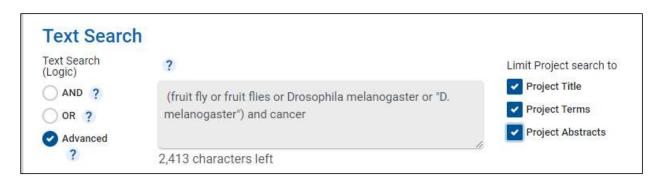
Finding NIH-Funded Projects Related to Research Organisms



Finding NIH-Funded Projects: NIH RePORTER

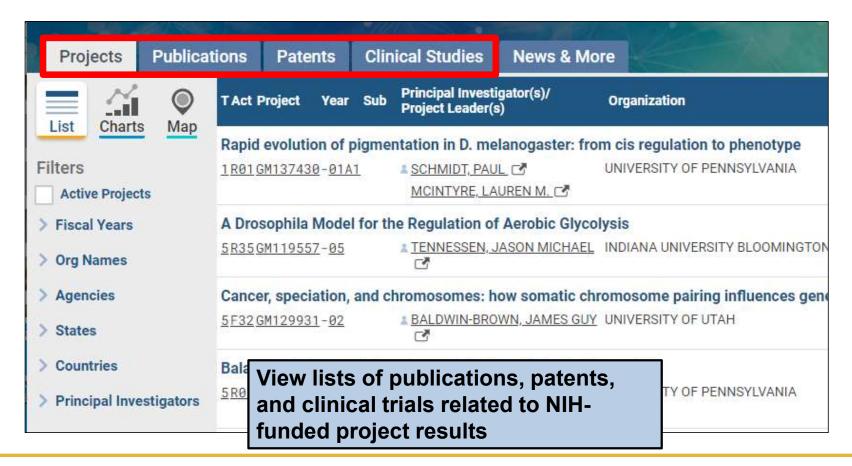


- Use <u>NIH RePORTER</u> (https://reporter.nih.gov/) to find NIH-funded research projects, investigators, publications, and patents
- Tips for locating projects that utilized specific research organisms:
 - Under <u>Advanced Projects Search</u> (https://reporter.nih.gov/advanced-search), choose Advanced text search
 - Enter all versions of the organism name (both common and scientific, as well as plural versions)
 - Use Boolean operators (AND/OR/NOT), quotes for phrases, and parentheses to group concepts
 - Example search: (fruit fly or fruit flies or Drosophila melanogaster or "D. melanogaster") and cancer
 - Try limiting text search to Project Title/Project Terms/Project Abstracts



Viewing Search Results on NIH RePORTER







Finding Genetic Information

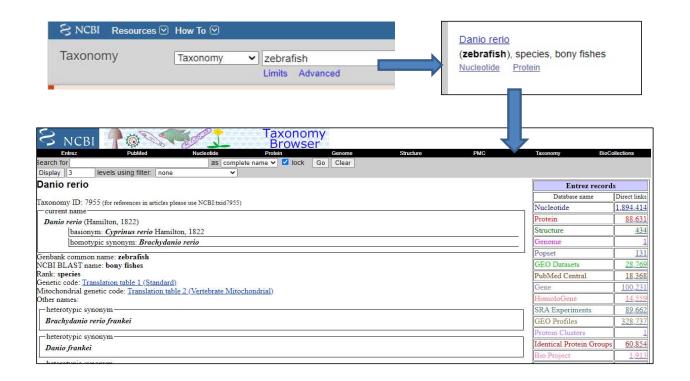


Using Taxonomy Browser



• Use the Taxonomy
Browser
(https://www.ncbi.nlm.nih.
gov/taxonomy) from the
National Center for
Biotechnology Information
(NCBI, part of the National
Library of Medicine) to
find links to genetic
information and
biomedical literature
related to specific
research organisms

 Search by common or scientific name





Using Taxonomy Browser: NCBI Database Links



Pages for specific organisms on Taxonomy Browser list direct links to other NCBI databases, such as:

- Nucleotide (genome, gene, and transcript sequence data)
- Protein (protein sequences)
- Genome (information on genomes including sequences, maps, chromosomes, assemblies, and annotations)
- PubMed Central (full-text biomedical articles)

Entrez records		
Database name	Direct links	
Nucleotide	1.894.414	
Protein	88.631	
Structure	434	
Genome	1	
Popset	131	
GEO Datasets	28.769	
PubMed Central	18.368	
Gene	100,231	
HomoloGene	14.559	
SRA Experiments	89,662	
GEO Profiles	328.737	
Protein Clusters	1	
Identical Protein Groups	60.854	
Bio Project	1.913	

Links to other NCBI databases for Danio rerio
(zebrafish) (https://bit.ly/3d1dRSM)





Using Taxonomy Browser: External Links



Pages for specific organisms on Taxonomy Browser also list links to external information resources, such as model organism databases

Links to external information resources for Danio rerio (zebrafish) (https://bit.ly/3d1dRSM)

External Information Resources (NCBI LinkOut)		
LinkOut	Subject	LinkOut Provider
DNA barcoding: Danio rerio	taxonomy/phylogenetic	Barcodes of Life
32 records from this provider	supplemental materials	Dryad Digital Repository
4 records from this provider	organism-specific	Genomes On Line Database
Show Biotic Interactions	taxonomy/phylogenetic	Global Biotic Interactions
Related Immune Epitope Information	gene/protein/disease-specific	Immune Epitope Database and Analysis Resource
639469800: Danio rerio Tuebingen	organism-specific	Integrated Microbial Genomes
Danio rerio (Hamilton, 1822)	taxonomy/phylogenetic	Integrated Taxonomic Information System
Dania sasia	taxonomy/phylogenetic	<u>Lifemap</u>
Zebrafish Model Organism Database	taxonomy/phylogenetic	NCBI taxonomy bookmarks
	taxonomy/phylogenetic	OMA Browser: Orthologous MAtrix



Examples of Model Organism Databases



- Many free model organism databases (MODs) are available to provide biological data for commonly used model organisms, such as:
 - FlyBase (http://flybase.org/) Fruit fly
 - Mouse Genome Informatics (MGI) (http://www.informatics.jax.org/) Mouse
 - Rat Genome Database (RGD) (https://rgd.mcw.edu/) Rat
 - Zebrafish Information Network (ZFIN) (http://zfin.org/) Zebrafish
- Generic Model Organism Database project (http://gmod.org/wiki/Main_Page) Toolkit of resources for creating/maintaining a MOD











Locating Model Organism Databases



Tips for locating model organism databases:

- Check the External Information Resources for organism pages on <u>Taxonomy Browser</u> (https://www.ncbi.nlm.nih.gov/taxonomy)
- Check the Online Bioinformatics Resources Collection
 (OBRC) by the Health Sciences Library System at the University
 of Pittsburgh (note that some links may be outdated):
 - Non-human vertebrates model organisms genomic databases (https://bit.ly/3o1BPU4)
 - Non-vertebrates model organisms genomic databases (https://bit.ly/2ZxY76r)



Overview



- Model organisms are often used as animal models in the study of human diseases
- Be aware of NIH Model Organism Sharing Policy
- Find information on animal models and model organisms through:
 - PubMed (biomedical articles)
 - Espacenet (patent information)
 - NIH RePORTER (NIH-funded research projects)
 - Taxonomy Browser (links to genetic information and biomedical literature)
 - Model organism databases (genetic information)





Questions?



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Questions?



Next OLAW Online Seminar: TBD March 2022

