Genomika a LZ

- ✓ Komparativní genomika
- ✓ Definice a standardizace kmenů na úrovni celých genomů

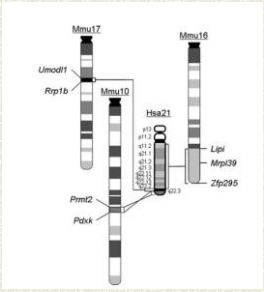
1

Komparativní genomika a LZ

- ✓ *Genomy LZ*
- ✓ *Genové manipulace a editace genomu LZ*

2

Připomenutí:
Myš jako model Downova syndromu



➢ https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2893810/

3

Genomika a LZ

- ✓ Komparativní genomika
- ✓ Definice a standardizace kmenů na úrovni celých genomů

4

Zvířecí (animální) laboratorní modely

- *Nematoda*
- *Dánio*
- *Drosophila*
- *Ptáci, hlodavci, domácí zvířata, lidoopi*

5

Netradiční laboratorní modely

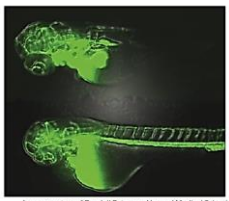
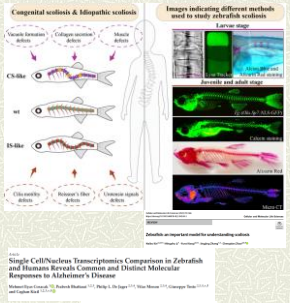


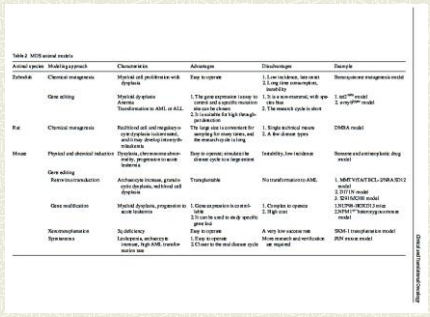
Image courtesy of Randall Peterson, Harvard Medical School and Massachusetts General Hospital, Boston, MA.

Fluorescent microangiograms of zebrafish homozygous for the gridlock mutation, which models human coarctation of the aorta. The vascular defect apparent in the upper embryo has been corrected in the lower embryo by treatment with the small molecule GS4012.



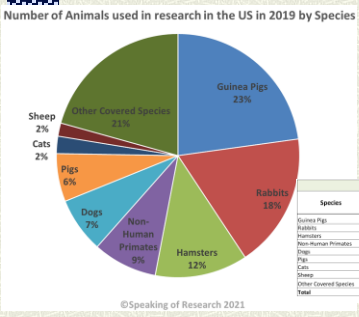
6

Netradiční laboratorní modely



7

Využití LZ (USA)



Animal Research in the US in 2019

Species	Number of Animals	% of Total	% Change from 2018
Guinea Pigs	181,993	22.8%	6%
Rabbits	142,472	17.9%	7%
Hamsters	96,296	12.3%	22%
Non-Human Primates	68,257	8.6%	-4%
Dogs	58,511	7.3%	-1%
Pigs	50,777	6.4%	1%
Cats	18,270	2.3%	2%
Sheep	13,953	1.7%	7%
Other Covered Species	165,017	20.7%	-10%
Total	797,546	100%	2.2%

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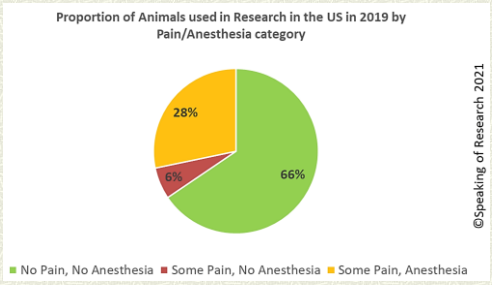
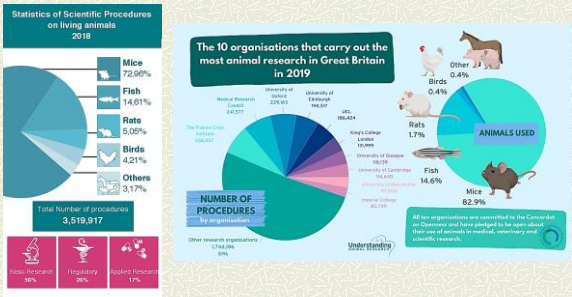
Využití LZ (USA procedures)



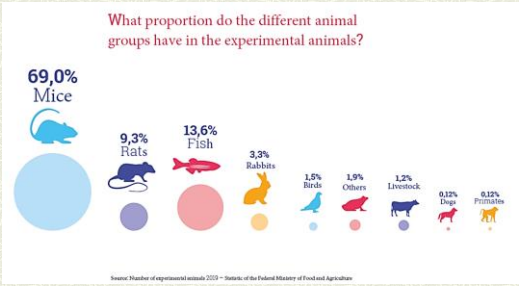
9

Využití LZ (UK)



10

Využití LZ (DE)



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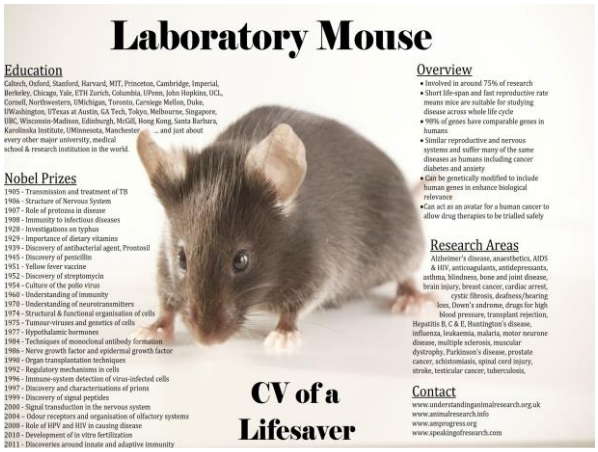
Zvířecí (animální) laboratorní modely

- *Nematoda*
- *Dánio*
- *Drosophila*
- *Ptáci, hlodavci, domácí zvířata, lidoopi*

12



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Myší model

- ✓ *Druhý sekvenovaný savčí genom (2002)*
- ✓ *Pravidla a nomenklatura*
- *http://www.informatics.jax.org/*
- ✓ *Databáze*

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Významné stránky

TABLE 1 Selected Genetic and Strain Databases Available on the World Wide Web (WWW)

Site	Contents	Web address (URL)
Mouse Genome Database	Mapping data (all techniques) genetic, cytogenetic, physical, and comparative mapping data	http://www.informatics.jax.org
MRC[a] Mammalian Genetics Unit	Comparative maps, strain list	http://www.mgu.har.mrc.ac.uk/
The Whole Mouse Catalog (formerly Mice and Rats Home Page)	Links to web sites for mouse and rat research	http://www.rodentia.com/wmc
Animal Genome Database in Japan	Mouse genetic mapping data, cytogenetic maps	http://ws4.niai.affrc.go.jp/
Human Genome Database[b]	Human gene symbols	http://bioinfo.sickKids.on.ca/http://gdbwww.gdb.org/
Human Gene Nomenclature Database	Human gene symbols	http://www.gene.ucl.ac.uk/cgi-bin/nomenclature/searchgenes.pl
National Center for Biotechnology Information (NCBI)	Mouse/human comparative maps, links to other databases	http://www.ncbi.nlm.nih.gov/Homology/
Rat Genome Database	Rat genetics	http://ratmap.gen.gu.se/
Roslin Institute Bioinformatics	Pig, sheep, cattle, chicken	http://www.ri.bbsrc.ac.uk/bioinformatics/
FlyBase	*Drosophila* genomics	http://flybase.bio.indiana.edu http://shigen.lab.nig.ac.jp/7081
Zebrafish Informatics	Zebrafish genomics	http://zfish.uoregon.edu/ZFIN/

a MRC, Medical Research Council.
b Note: At the time of this writing, the Human Genome Database is in transition between the two sites listed.

https://www.informatics.jax.org/

From: Genetic and Phenotypic Definition of Laboratory Mice and Rats / What Constitutes an Acceptable Genetic-Phenotypic Definition

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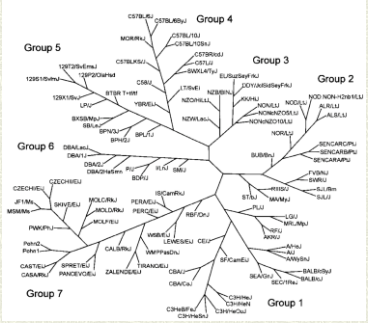
Genetika LZ: myší kmeny



Petkov et al. 2021

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Kmeny/linie LZ (myší/LZ)

International Mouse Strain Resource Center (IMSR)
http://www.findmice.org/

- ***Existující: >24.000***
- ***Potenciál: 200.000***

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Genetika LZ

Základní genetické rozdělení

- *Outbrední LZ*
- *Inbrední LZ*

18

Genetika LZ

Základní genetické rozdělení

- *Outbrední LZ*
- *Inbrední LZ*

19

Neinbrední kmeny myší

- ✓Outbred Stock (OUT)
- ✓Noninbred Stock (NON)
- ✓ Closed Colony (CCO)

#

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Genetika LZ

Základní genetické rozdělení

- Outbrední LZ
- Inbrední LZ

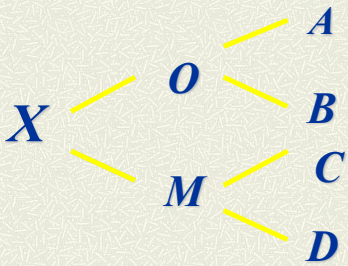
21

Inbríding

Jev, který nastává po páření příbuzných jedinců

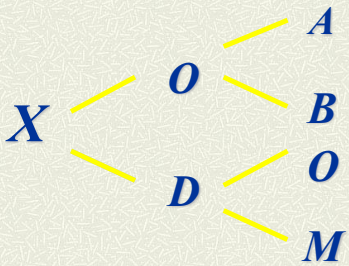
22

Inbríding



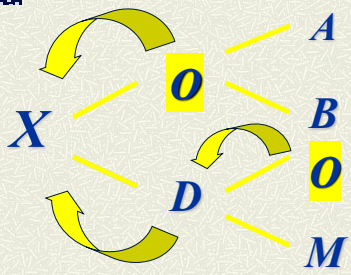
23

Inbríding



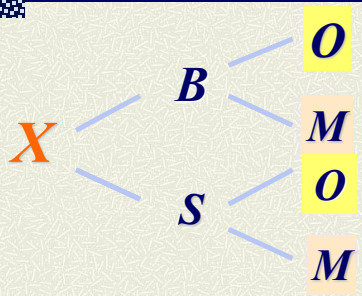
24

Inbríding



25

Inbríding



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Inbríding

- **Společný předek do 5. generace**
- **Homozygotnost**

27

Inbríding

- Účinky: *genotyp/genofond*
- Účinky: *fenotyp*

28

Inbríding: účinky na fenotyp

kmen Vandoma, Zimbabwe (tzv. „Pštrosí lidé"): ektrodaktylie
mormoni v Hilldale (Utah) a Colorado City (Arizona)
amazonští indiáni
šlechtické rody




Rudolf II. Karel II. Španělský František I.

Karel II.: nepřirozeně velká hlava, deformovaná čelist, slabé tělo, potíže s chůzí a další defekty, mentální a psychické poruchy, impotence, neplodnost.

https://slideplayer.cz/slide/5645547/6/images/28/inbredn%C3%AD+deprese+u+%C4%8Dlov%C4%9Bka%3A.jpg

29

Inbríding: účinky na fenotyp

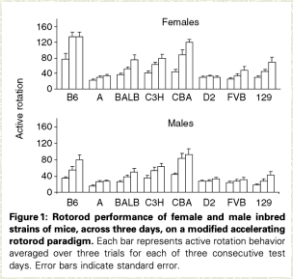

Figure 1: Rotorod performance of female and male inbred strains of mice, across three days, on a modified accelerating rotorod paradigm. Each bar represents active rotation behavior averaged over three trials for each of three consecutive test days. Error bars indicate standard error.

McFadyen et al. 2003

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Inbrední kmeny myší
základní rozdělení

- ✓ Syngenní (isogenní)
- ✓ Rekombinantní
- ✓ Koisogenní
- ✓ Kongenní
- ✓ Konsomické, konplastické
- ✓ Mutantní
- ✓ Knock-out
- ✓ Transgenní/s editovaným genomem

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Syngenní (isogenní) kmeny (IS)

AaBb

AABB AAbb aaBB aabb

32

Syngenní (isogenní) kmeny (IS)

- Vzniklé opakovaným pářením bratr x sestra (>20 x)
- Geneticky identické - isogenní
- 100% (?) homozygotní

33

Rekombinantní kmeny (RI)

AA bb x aa BB

AaBb

AABB AAbb aaBB aabb

Segregating Inbred Strains (SEG)

34

„Ko-“ kmeny

- Ko-izogenní: Coisogenic Strain (COI)
- Kongenní: Congenic Strain (CON)
- Konsomický: Consomic Strain (CSS)
- Konplastický Conplastic Strain (CSS)

35

Kongenní kmeny

- Vzniklé zpětnými kříženími
- Odlišnost v jediné oblasti (více lokusů)

36

Kongenní kmeny

A x B

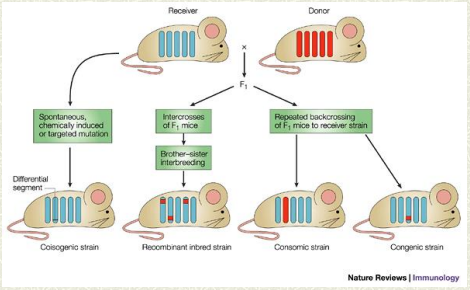
AB x B

ABB x B

ABBBBBBBBBBBBBBBBBBBB

37

Typy kmenů



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Mutantní kmeny

- Mutant Strain (MSR)
- Mutant Stock (MSK)

39

Jiné kmeny

- ✓ Wild-Derived Inbred Strains (WDS)
- ✓ Knock-out
- ✓ Transgenní/s editovaným genomem

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Kmeny LZ

Type	2021	2015	2010	2000
Mice, inbred strains	28559	29504	24403	11739
Mice, transgenic	11524	15653	14380	5739
Mice, knockout	7465	9742	9182	3400
Mice, congenic	28	28	111	44
Mice, none of above *	21587	34528	30080	16308

Table 2. Types of mice and the frequency of citations in PUBMED bibliographic database, as of July 8, 2022. As PUBMED continues to update its database, the number will change, especially for the most recent year. * *PUBMED search parameter: mice [mesh] NOT mice, inbred strains [mesh] NOT mice, transgenic [mesh] NOT mice, knockout [mesh] NOT mice, congenic [mesh].*

strain	major features	advantages	main applications
C57BL/6	inbred, black	strain stability, easy breeding	physiological or pathological models for *in vivo* experiments, background strain for transgenics and congenics
BALB/c	inbred, albino, immunodeficient	easy breeding, tumor-prone	hybridoma and monoclonal antibody production, research models for cancer therapy and immunology.
CD-1	outbred, albino	genetic variability	positional cloning, genotypic selection, toxicology testing (questionable)
CB17 SCID	inbred, albino	no T and B cells, tumor transplantation	immunodeficient animal model for testing new cancer treatments and as hosts for human immune system tissues.

Table 4. Major mouse strains, their features, and applications. Searches were done through MESH tree terms and NCBI MESH annotations.

Laboratory Mice and Rats

Mary Johnson (han at labome dot com)
Synatom Research, Princeton, New Jersey, United States

DOI //dx.doi.org/10.13070/mm.en.2.113
Date last modified : 2022-07-08; original version : 2012-10-05
Cite as MATER METHODS 2012;2:113

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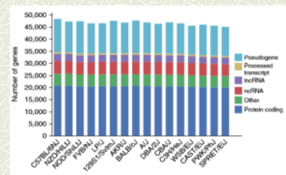
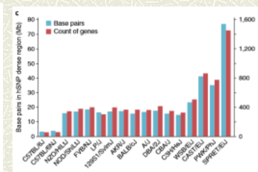
Genom myších kmenů

Nucleic Acids Res. 2002 Jan 1; 30(1): 113–115. PMCID: PMC99116
doi: 10.1093/nar/30.1.113 PMID: 11752269

The Mouse Genome Database (MGD): the model organism database for the laboratory mouse

Judith A. Blake,* Joel E. Richardson, Carol J. Bult, Jim A. Kadin, and Janan T. Eppig





ARTICLES

Sixteen diverse laboratory mouse reference genomes define strain-specific haplotypes and novel functional loci

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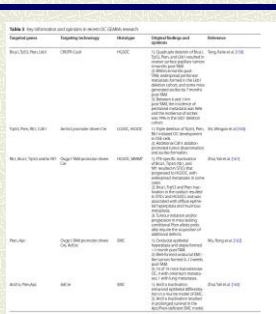
Geneticky modifikované myší modely



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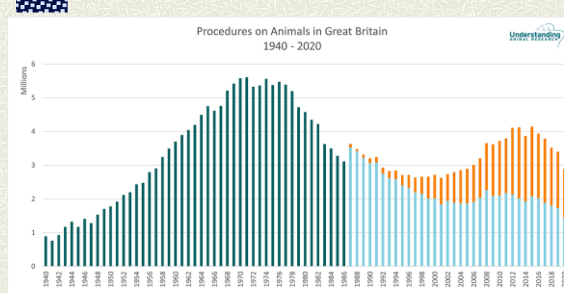
Využití LZ (USA)



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Příklad nabídky v ČR

Potkani

- ✓ Outbrední kmeny (8)
- ✓ Inbrední kmeny (4)
- ✓ Speciální kmeny (18)

Myši

- ✓ Outbrední kmeny (7)
- ✓ Inbrední kmeny (9)
- ✓ Hybridní kmeny (4)
- ✓ Speciální kmeny (5)
- ✓ Imunodeficientní kmeny (9)
- ✓ JAX (1)

https://www.greenpets.cz%2Fpotkan-laboratorni%2F&psig=AOvVaw3ZryX46oXhTasMU26y9qR&ust=1646131607036000&source=images&cd=vfe&ved=0CAsQjRxqFwoTCLjMwNKcovYCFQAAAAAdAAAAABAD

Ostatní druhy (křeček zlatý, morče, králík, pískomil)

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Využití kmenů LZ

- ✓ Standardizace
- ✓ Biomodely
- ✓ Etika pokusů na zvířatech

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Využití kmenů LZ

- ✓ Standardizace
- ✓ Biomodely
- ✓ Etika pokusů na zvířatech

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Myš jako model lidských onemocnění

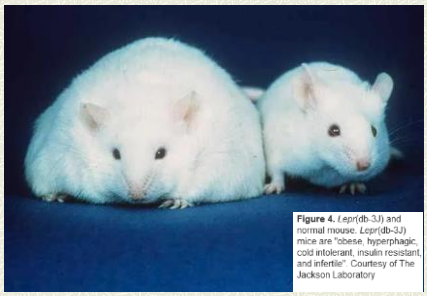

Figure 4. *Lepr*(db-3J) and normal mouse. *Lepr*(db-3J) mice are "obese, hyperphagic, cold intolerant, insulin resistant, and infertile". Courtesy of The Jackson Laboratory

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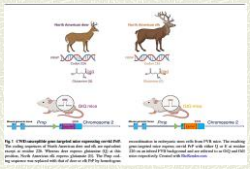
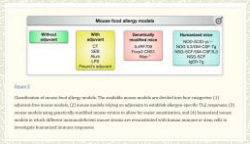
Specifické myší modely





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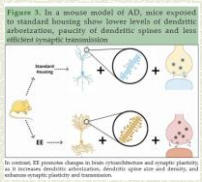
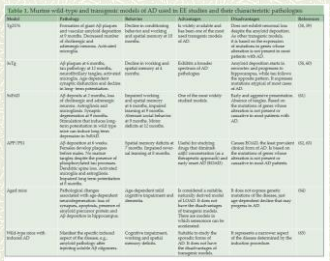
Specifické myší modely





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Využití kmenů LZ

- ✓ Standardizace
- ✓ Biomodely
- ✓ Etika pokusů na zvířatech

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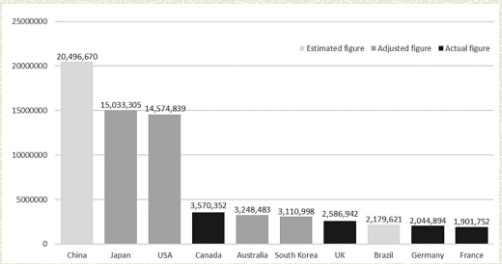
Využití LZ



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Etika pokusů na zvířatech

https://www.enviweb.cz/tmp/thumbnails/712/f2/f22419cca6ccefce6c47498ed8c1b298.jpg

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