PS2-4

Quality and Quantity Matter in Disease Model Curation

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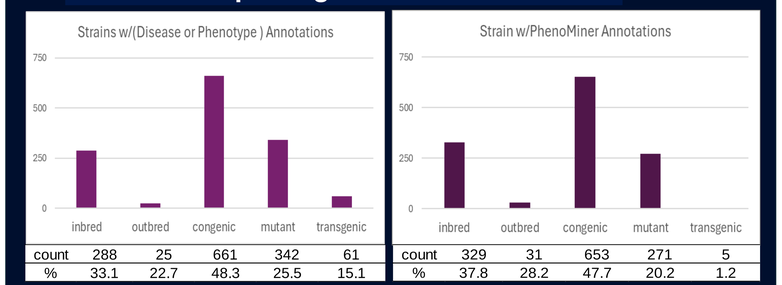
https://rgd.mcw.edu

Abstract

Rats have been used in disease research for over 100 years. These disease models arise from naturally occurring mutations, selective breeding and, more recently, genome manipulation. To better curate rat strains and keep up with the variety of strains generated by genome editing, the RGD curation team has revisited strain curation to specifically annotate disease model strains from published literature. The MODEL qualifier is used in conjunction with the disease ontology term to highlight the annotated strain as a disease model. Information such as how the model is produced or what aspect of the disease this model is used for are also curated. The disease model strains are characterized by several disease-associated phenotypes and/or have been reported in several publications where the same disease was studied. The quantitative phenotypes of these model strains can be accessed from the PhenoMiner links provided in the strain report page and their phenotype relative to other rat strains can be found through the Expected Ranges tool. The damaging variants are available in the strain report page if the strain was sequenced, and the full genome variation analysis can be found in the Variant Visualizer tool. Linking disease/phenotype annotation and genomic variations of the disease model will provide a useful approach to understanding the complexities of physiological genomics.

Exploring Rat Models



	inbred	outbred	congenic	mutant	transgenic
count	288	25	661	342	61
%	33.1	22.7	48.3	25.5	15.1

	inbred	outbred	congenic	mutant	transgenic
count	329	31	653	271	5
%	37.8	28.2	47.7	20.2	1.2

Strain Report

Strain: SS-*Nppb*$^{em2Mcwi-/-}$

Symbol:	SS-*Nppb*$^{em2Mcwi-/-}$
Strain:	SS-*Nppb*$^{em2-}$/*Nppb*$^{em2-}$
Substrain:	Mcwi
Full Name:	SS-*Nppb*$^{em2Mcwi-}$/*Nppb*$^{em2Mcwi-}$
RGD ID:	5686730
Citation ID:	RRID:RGD_5686730
Ontology ID:	RS:0003075
Alleles:	Nppb^{em2Mcwi}
Also Known As:	SS-Nppbem2Mcwi-/-; SS-Nppbem2Mcwi/1Mcwi; SS-Nppb^{em2Mcwi}/1Mcwi; SS-Nppbem2Mcwi-/Nppbem2Mcwi-; SS-Nppb^[em2Mcwi-/-]
Type:	mutant

RGD Manual Disease Annotations *Click to see Annotation Summary View*

☐ **Only show annotations with direct experimental evidence (0 objects hidden)**

Object Symbol	Species	Term	Qualifier	Evidence	With	Reference	Notes	Source	Original Reference(s)
SS-*Nppb*$^{em2Mcwi-/-}$	Rat	Hypertensive Nephropathy	MODEL: age-related	IMP		12910116		RGD	

Mammalian Phenotype

Object Symbol	Species	Term	Qualifier	Evidence	With	Reference	Notes	Source	Original Reference(s)
SS-*Nppb*$^{em2Mcwi-/-}$	Rat	cardiac hypertrophy		IMP		12910116		RGD	
SS-*Nppb*$^{em2Mcwi-/-}$	Rat	hypertension		IMP		12910116		RGD	
SS-*Nppb*$^{em2Mcwi-/-}$	Rat	increased urine protein level		IMP		12910116		RGD	
SS-*Nppb*$^{em2Mcwi-/-}$	Rat	prolonged QT interval		IMP		12910116		RGD	

- All disease and phenotype annotations are displayed with the references in the strain report page.
- The quantitative phenotype values are cataloged into four ontologies.
- Each selection is linked out to the PhenoMiner tool where results are shown as a bar chart.

Phenotype Values via Phenominer *Click to see Annotation Summary View*

Related Phenotype Data for Term "SS-Nppbem2Mcwi-/-" (RS:0003075)

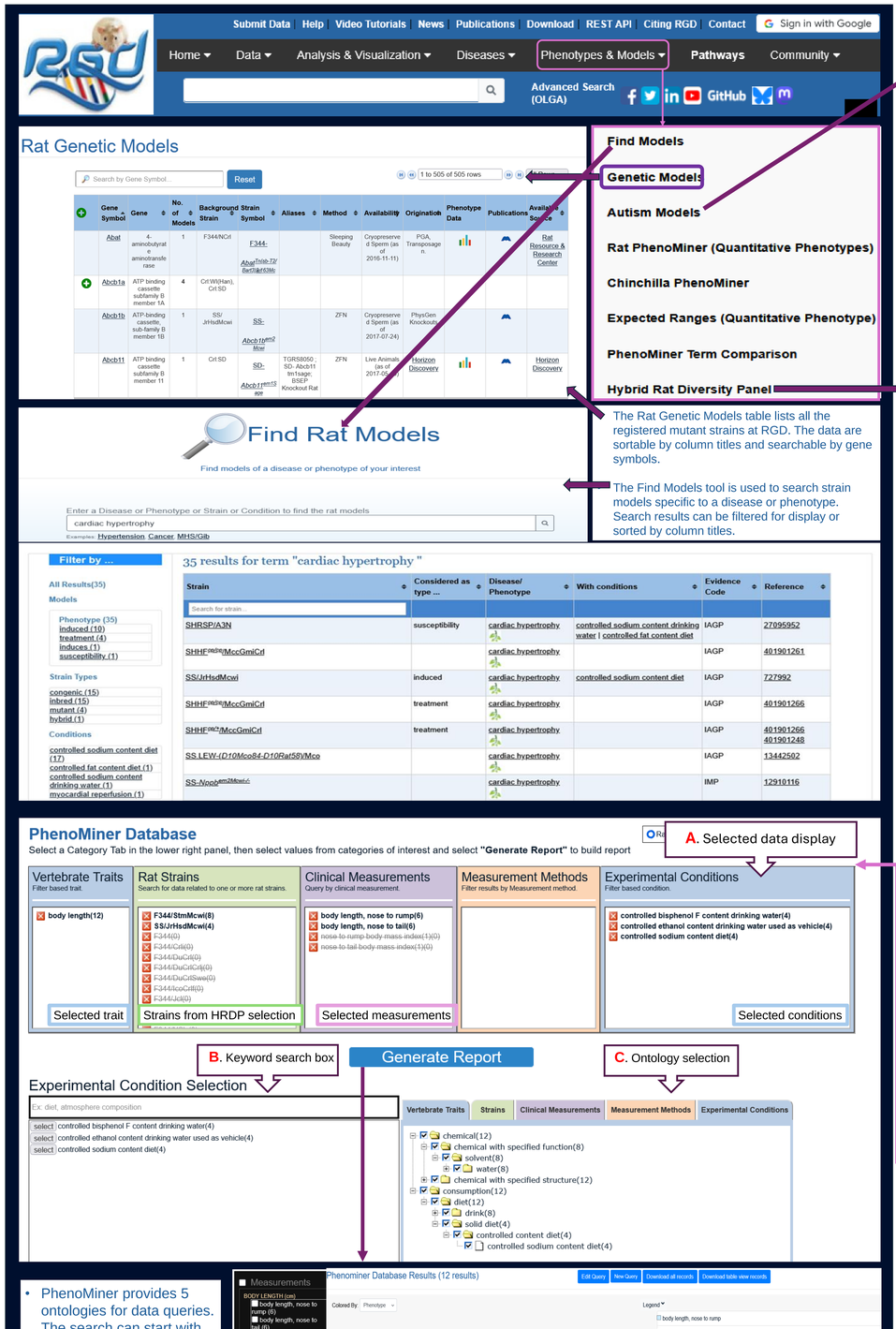
Rat Strains:
- SS-Nppbem2Mcwi-/-

Clinical Measurements:
- blood glucose level
- blood hemoglobin level
- blood urea nitrogen level
- body weight
- diastolic blood pressure
- ejection fraction
- heart interventricular end-diastolic septal wall

Experimental Conditions:
- control condition
- controlled sodium chloride content diet
- controlled sodium content diet
- gene transfer of the rat natriuretic peptide B gene using an adenovirus vector
- vehicle control condition

Measurement Methods:
- automated blood cell counting method
- automated hematology analysis
- automated platelet count test
- autom
- autom analys
- autom

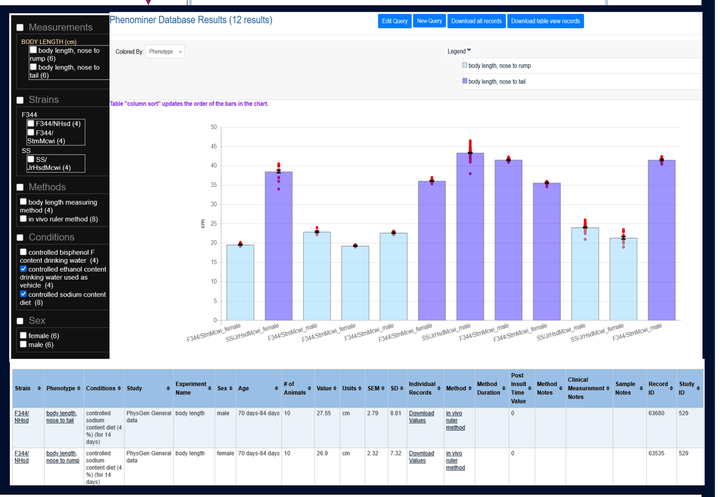
- The black panel on the left allows filtration of diastolic blood pressure data.
- Each bar represents the mean and SD curated from a publication or data submission. Bars are color-coded with conditions.
- Data associated with the displayed chart are viewable and downloadable at the table at the bottom.



PhenoMiner Database

Select a Category Tab in the lower right panel, then select values from categories of interest and select **"Generate Report"** to build report

- PhenoMiner provides 5 ontologies for data queries. The search can start with any ontology of interest in any order.
- Keyword search is available in (**B**) & ontology browsing in (**C**). The selected data are displayed on the top panel (**A**).
- "Generate Report" tab creates results page in a new tab that allows easy going back to edit queries.
- Two kinds of body lengths, nose to rump and nose to tail, are displayed in the same graph coded with different colors. The left black panel allows more filtration of data.



Strain	Phenotype	Conditions	Study	Experiment Name	Sex	Age	# of Animals	Value	Units	SEM	SD	Individual Records	Method	Method Duration	Post Insult Time Value	Method Notes	Clinical Measurement Notes	Sample Notes	Record ID	Study ID
F344/NHsd	body length, nose to tail	controlled sodium content diet (4 %) (for 14 days)	PhysiGen General data	body length	male	70 days-84 days	10	27.55	cm	2.79	8.81	Download Values	in vivo ruler method		0				63680	529
F344/NHsd	body length, nose to rump	controlled sodium content diet (4 %) (for 14 days)	PhysiGen General data	body length	female	70 days-84 days	10	26.9	cm	2.32	7.32	Download Values	in vivo ruler method		0				63535	529

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Autism Rat Model Resource

Laboratory rats are the animal of choice in neurobiology, with a more complex behavioral repertoire than mice and a larger brain permitting more sophisticated electrophysiological recordings. Recent developments in gene editing technologies have now allowed the development of genetically linked disorders.

The Medical College of Wisconsin has been working with the Simons Foundation Autism Research Initiative (SFARI) to generate and distribute engineered rat models of autism. Models will be maintained in the outbred Long-Evans (Crl:LE) background strain, as this is often the strain of choice for cognitive, behavioral and systems neuroscience studies. These models are available to any qualified researcher for non-commercial research, with minimal cost and restrictions.

Available Strains

Model	Strain name	RGDID
Fmr1 knockout (m2)	LE-*Fmr1*^{em2Mcwi}	11553873
Arid1b knockout	LE-*Arid1b*^{em1Mcwi}	14394518
Grin2b knockout	LE-*Grin2b*^{em1Mcwi}	14394515
Dyrk1a knockout (m3)	LE-*Dyrk1a*^{em3Mcwi}	25394526
Scn2a knockout (m1)	LE-*Scn2a*^{em1Mcwi}	25394530
Chd8 knockout (m1)	LE-*Chd8*^{em1Mcwi}	25330088
Cntnap2 knockout (m1)	LE-*Cntnap2*^{em1Mcwi}	25330087
Nrxn1 knockout (m1)	LE-*Nrxn1*^{m1Mcwi}	25330089

The Hybrid Rat Diversity Panel

The Hybrid Rat Diversity Panel (HRDP) consists of 96 inbred rat strains with genetic and phenotypic diversity . Many of the HRDP strains are currently available for experiments (HRDP@mcw.edu). Phenotype annotations and whole genome sequence data are available for analysis through the Portal.

Contact HRDP

HRDP strains are listed below. To explore PhenoMiner or Variant Visualizer data, check strain(s) and "analyze".

Classic Inbred Strains

	Strain	Strain Available	Phenominer Data	Variant Visualizer Data
☐	ACI	ACI/EurMcwi	✓	✓
☐	BDIX	BDIX/NemOdaMcwi	✓	✓
☐	BN	BN/NHsdMcwi	✓	✓
☐	BN-*Lx*	BN-*Lx*/CubMcwi	✓	✓

HXB/BXH Recombinant Inbred Panel Strains

	Strain	Strain Available	Phenominer Data	Variant Visualizer Data
☐	BN-*Lx*	BN-*Lx*/CubMcwi	✓	✓
☑	BXH10/Cub		✗	✗
☐	BXH11/Cub		✗	✗
☐	BXH12/Cub	BXH12/CubMcwi	✗	✗
☐	BXH13/Cub	BXH13/CubMcwi	✗	✗
☐	BXH2/Cub	BXH2/CubMcwi	✓	✓
☐	BXH3/Cub		✗	✓
☐	BXH5/Cub		✗	✗

FXLE/LEXF Recombinant Inbred Panel Strains

	Strain	Strain Available	Phenominer Data	Variant Visualizer Data
☑	F344	F344/StmMcwi	✓	✓
☑	FXLE12/Stm	FXLE12/StmMcwi	✓	✓
☐	FXLE13/Stm	FXLE13/StmMcwi	✓	✓
☐	FXLE14/Stm	FXLE14/StmMcwi	✓	✓
☐	FXLE15/Stm	FXLE15/StmMcwi	✓	✓
☐	FXLE16/Stm	FXLE16/StmMcwi	✓	✓
☐	FXLE17/Stm	FXLE17/StmMcwi	✓	✓
☐	FXLE18/Stm	FXLE18/StmMcwi	✓	✓

Analyze