Enhanced Hybrid Rat Diversity Panel (HRDP) resources at RGD

Mary Kaldunski

20th Annual Meeting of the Complex Trait Community | Rat Genome & Models

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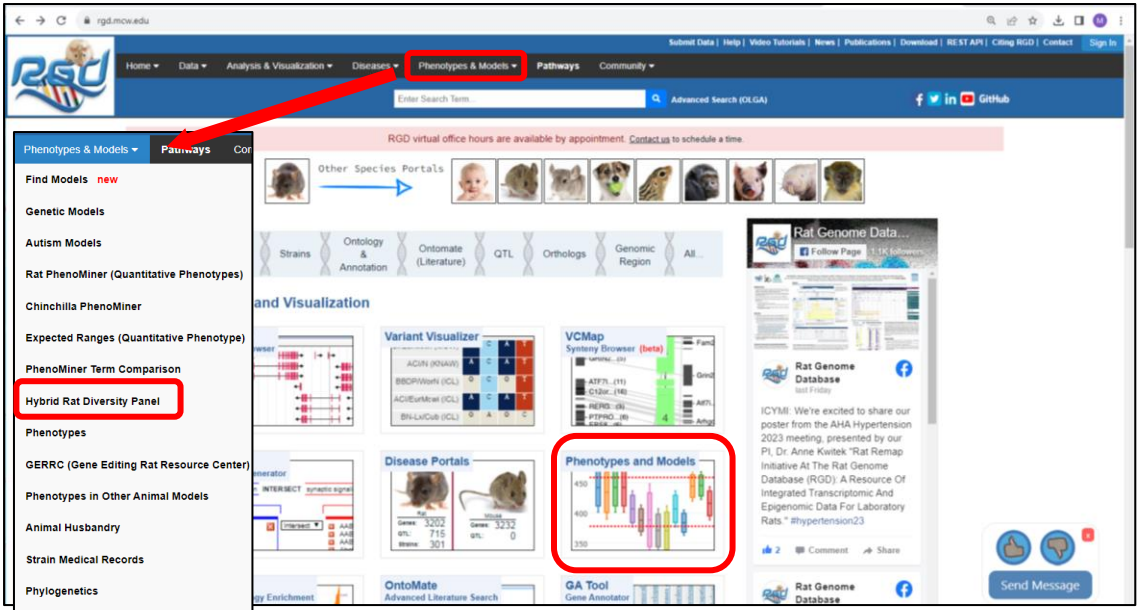
https://rgd.mcw.edu

The Hybrid Rat Diversity Panel

- Includes a broad selection of classical inbred strains and two recombinant inbred panels
- Is designed to maximize genetic and phenotypic diversity
- Also maximizes the power to detect and fine-map genetic loci associated with complex traits
- At MCW is a funded program to rederive, sequence, maintain, and **distribute** the HRDP strains, including available Heterogeneous Stock (HS) founder strains

The Hybrid Rat Diversity Panel



The HRDP information is organized on a portal page which is accessible from either the Phenotypes & Models dropdown menu, or from the Phenotypes and Models option on the RGD homepage.

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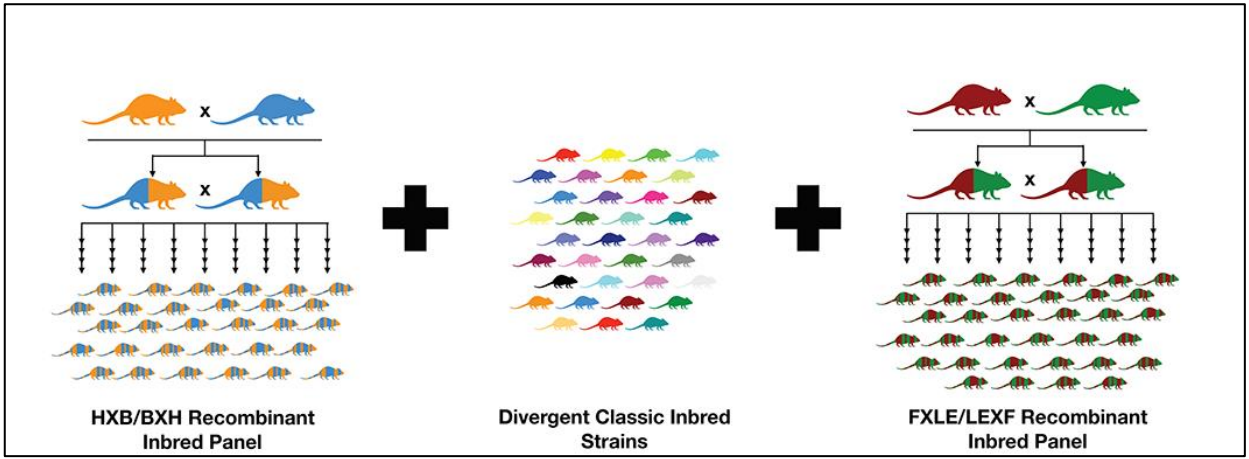

The HRDP portal page provides a description of the construction and format of the panel. Image courtesy of Dr. Saba.

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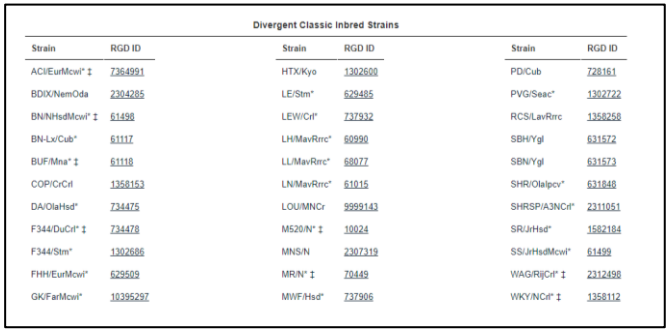
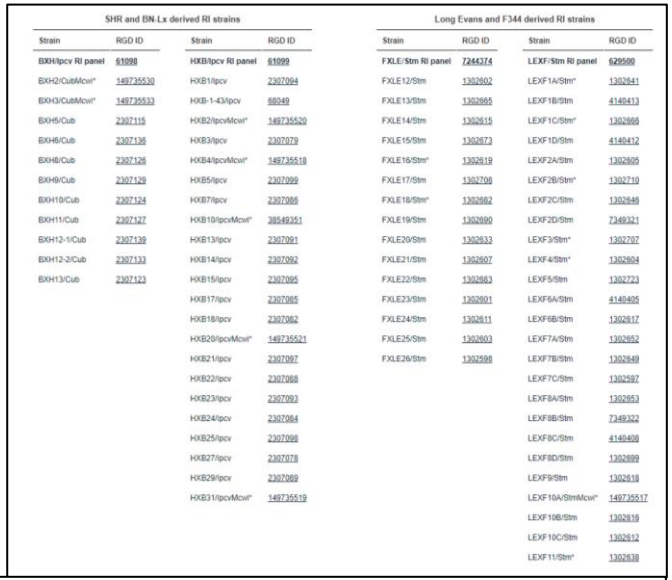


Divergent Classic Inbred Strains

Strain	RGD ID	Strain	RGD ID	Strain	RGD ID
ACI/EurMcwi* ‡	7364991	HTX/Kyo	1302600	PD/Cub	728161
BDIX/NemOda	2304285	LE/Stm*	629485	PVG/Seac*	1302722
BN/NHsdMcwi* ‡	61498	LEW/Crl*	737932	RCS/LavRrrc	1358256
BN-Lx/Cub*	61117	LH/MavRrrc*	60990	SBH/Ygl	631572
BUF/Mna* ‡	61118	LL/MavRrrc*	68077	SBN/Ygl	631573
COP/CrCrl	1358153	LN/MavRrrc*	61015	SHR/OlaIpcv*	631848
DA/OlaHsd*	734475	LOU/MNCr	9999143	SHRSP/A3NCrl*	2311051
F344/DuCrl* ‡	734478	M520/N* ‡	10024	SR/JrHsd*	1582184
F344/Stm*	1302686	MNS/N	2307319	SS/JrHsdMcwi*	61499
FHH/EurMcwi*	629509	MR/N* ‡	70449	WAG/RijCrl* ‡	2312498
GK/FarMcwi*	10395297	MWF/Hsd*	737906	WKY/NCrl* ‡	1358112



SHR and BN-Lx derived RI strains

Strain	RGD ID	Strain	RGD ID
BXH/Ipcv RI panel	61098	HXB/Ipcv RI panel	61099
BXH2/CubMcwi*	149735530	HXB1/Ipcv	2307094
BXH3/CubMcwi*	149735533	HXB-1-43/Ipcv	68049
BXH5/Cub	2307115	HXB2/IpcvMcwi*	149735520
BXH6/Cub	2307136	HXB3/Ipcv	2307079
BXH8/Cub	2307126	HXB4/IpcvMcwi*	149735518
BXH9/Cub	2307129	HXB5/Ipcv	2307099
BXH10/Cub	2307124	HXB7/Ipcv	2307086
BXH11/Cub	2307127	HXB10/IpcvMcwi*	38549351
BXH12-1/Cub	2307139	HXB13/Ipcv	2307091
BXH12-2/Cub	2307133	HXB14/Ipcv	2307092
BXH13/Cub	2307123	HXB15/Ipcv	2307095
		HXB17/Ipcv	2307085
		HXB18/Ipcv	2307082
		HXB20/IpcvMcwi*	149735521
		HXB21/Ipcv	2307097
		HXB22/Ipcv	2307088
		HXB23/Ipcv	2307093
		HXB24/Ipcv	2307084
		HXB25/Ipcv	2307096
		HXB27/Ipcv	2307078
		HXB29/Ipcv	2307089
		HXB31/IpcvMcwi*	149735519

Long Evans and F344 derived RI strains

Strain	RGD ID	Strain	RGD ID
FXLE/Stm RI panel	7244374	LEXF/Stm RI panel	629500
FXLE12/Stm	1302602	LEXF1A/Stm*	1302641
FXLE13/Stm	1302665	LEXF1B/Stm	4140413
FXLE14/Stm	1302615	LEXF1C/Stm*	1302666
FXLE15/Stm	1302673	LEXF1D/Stm	4140412
FXLE16/Stm*	1302619	LEXF2A/Stm	1302605
FXLE17/Stm	1302706	LEXF2B/Stm*	1302710
FXLE18/Stm*	1302682	LEXF2C/Stm	1302646
FXLE19/Stm	1302690	LEXF2D/Stm	7349321
FXLE20/Stm	1302633	LEXF3/Stm*	1302707
FXLE21/Stm	1302607	LEXF4/Stm*	1302604
FXLE22/Stm	1302683	LEXF5/Stm	1302723
FXLE23/Stm	1302601	LEXF6A/Stm	4140405
FXLE24/Stm	1302611	LEXF6B/Stm	1302617
FXLE25/Stm	1302603	LEXF7A/Stm	1302652
FXLE26/Stm	1302598	LEXF7B/Stm	1302649
		LEXF7C/Stm	1302597
		LEXF8A/Stm	1302653
		LEXF8B/Stm	7349322
		LEXF8C/Stm	4140408
		LEXF8D/Stm	1302699
		LEXF9/Stm	1302618
		LEXF10A/StmMcwi*	149735517
		LEXF10B/Stm	1302616
		LEXF10C/Stm	1302612
		LEXF11/Stm*	1302638

The original strains are listed on the portal page and noted (*) for those that have been sequenced to date and loaded to Variant Visualizer (VV). Almost twice as many strains have been sequenced and will be available in VV soon.
VCF files are available for download for all the sequenced strains.

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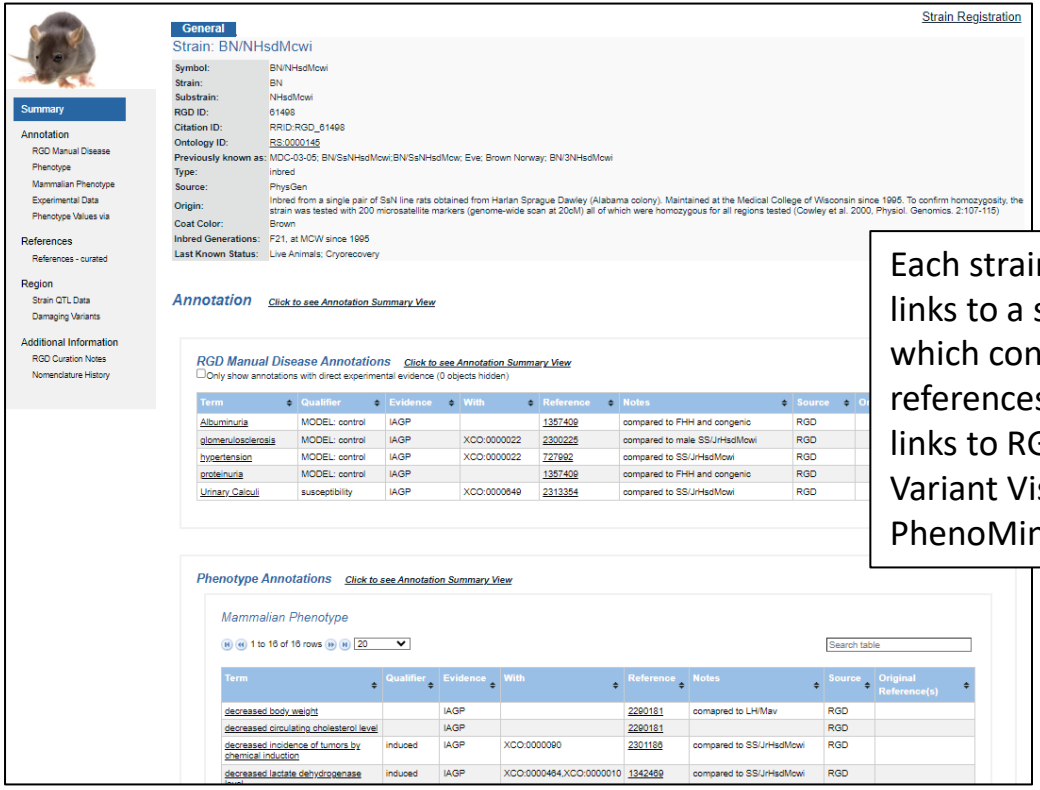

Each strain has an RGD ID that links to a strain report page which contains annotations, references, QTLs, and further links to RGD tools such as Variant Visualizer (VV) and PhenoMiner.

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Some of the information available at RGD for the HRDP strains includes:
228 curated references with RGDIDs, for disease and MP annotations
101 qualitative disease annotations for 41 HRDP strains
226 mammalian phenotype annotations for 45 HRDP strains
108 studies curated in PhenoMiner that include 65 HRDP strains
10,680 quantitative phenotype records for those studies
13,904,382 variants loaded in VV for 41 HRDP strains to date

HS Founder Strain	HRDP Best Match	Genetic Similarity
ACI/N	ACI/EurMcwi	0.997
BN/SsN	BN/NHsdMcwi	0.999
BUF/N	BUF/Mna	0.736
F344/N	F344/DuCrl	0.995
M520/N	M520/NRrrcMcwi	0.997
MR/N	MR/NRrrc	0.998
WKY/N	WKY/NHsd	0.997
	WKY/NCrl	0.971
WN/N	WAG/RijCrl	0.720

The genetic similarity between Heterogeneous Stock (HS) founder strains and the best match strain in the HRDP has been quantified (Drs. Chen, Palmer and colleagues).

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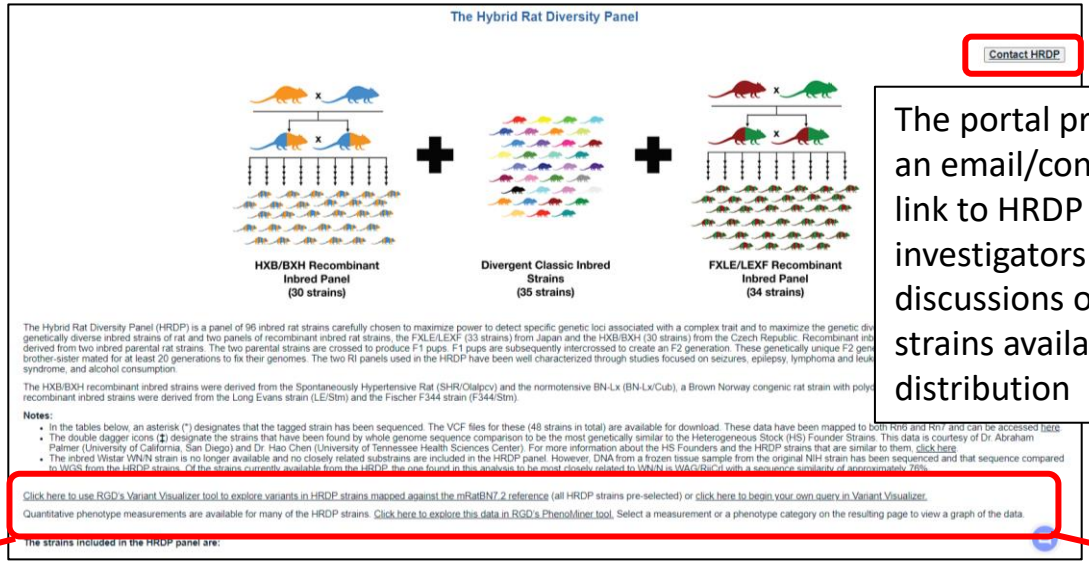

The portal provides an email/contact link to HRDP investigators for discussions of strains available for distribution

Click here to use RGD's Variant Visualizer tool to explore variants in HRDP strains mapped against the mRatBN7.2 reference (all HRDP strains pre-selected) or click here to begin your own query in Variant Visualizer.
Quantitative phenotype measurements are available for many of the HRDP strains. Click here to explore this data in RGD's PhenoMiner tool. Select a measurement or a phenotype category on the resulting page to view a graph of the data.

The HRDP portal provides links to Variant Visualizer and PhenoMiner for HRDP specific data. The advantage of these links is that available strains are preselected in the tools.

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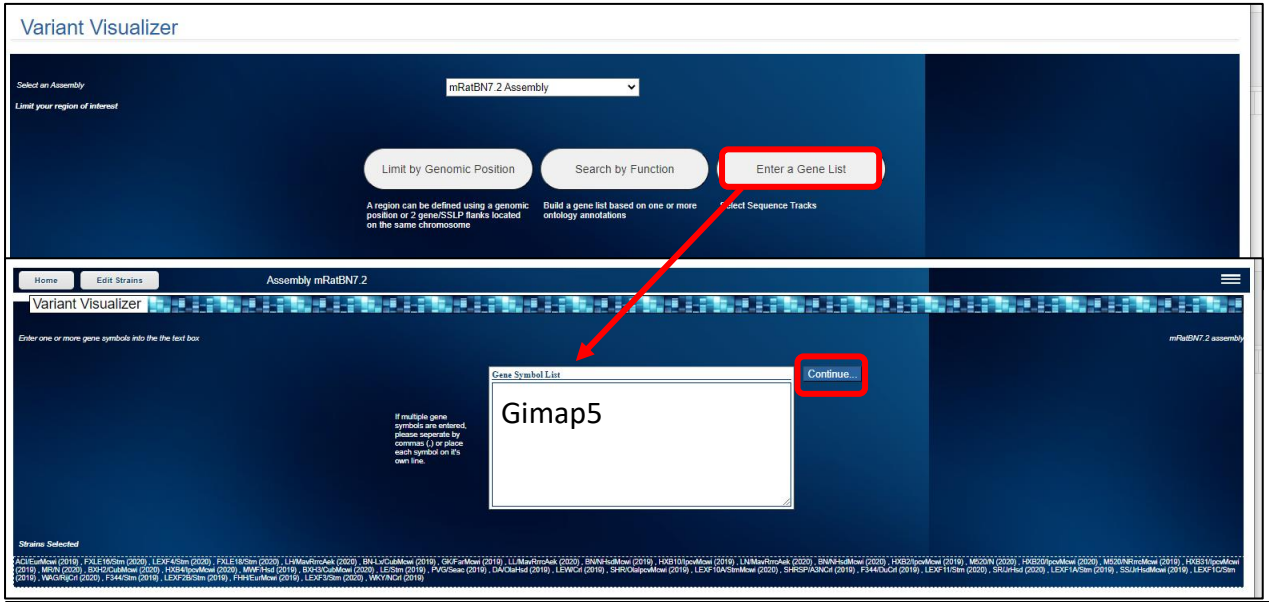

The Variant Visualizer option from the HRDP portal page will open with available strains preselected. Enter a gene ID and click Continue to generate a display of variants for the input strains and gene(s).

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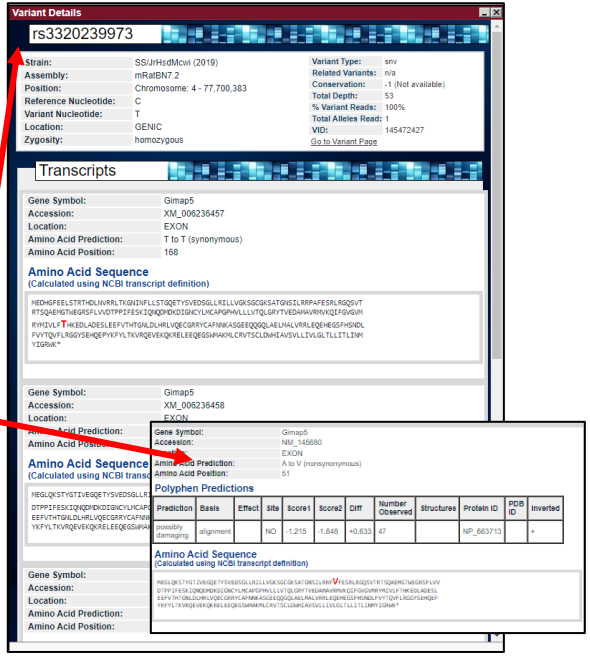
Selecting a particular variant will open a Variant Details report.



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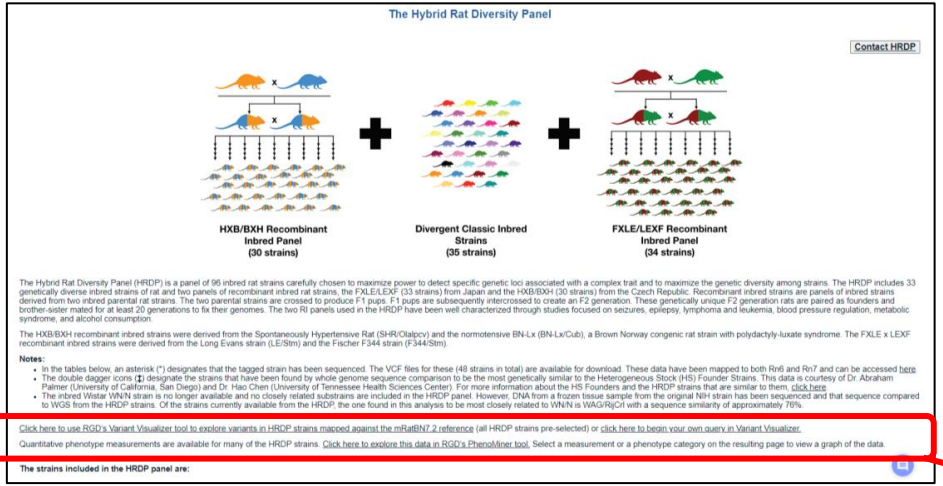

Click here to use RGD's Variant Visualizer tool to explore variants in HRDP strains mapped against the mRatBN7.2 reference (all HRDP strains pre-selected) or click here to begin your own query in Variant Visualizer.
Quantitative phenotype measurements are available for many of the HRDP strains. Click here to explore this data in RGD's PhenoMiner tool. Select a measurement or a phenotype category on the resulting page to view a graph of the data.

Another option on the HRDP portal page was PhenoMiner.

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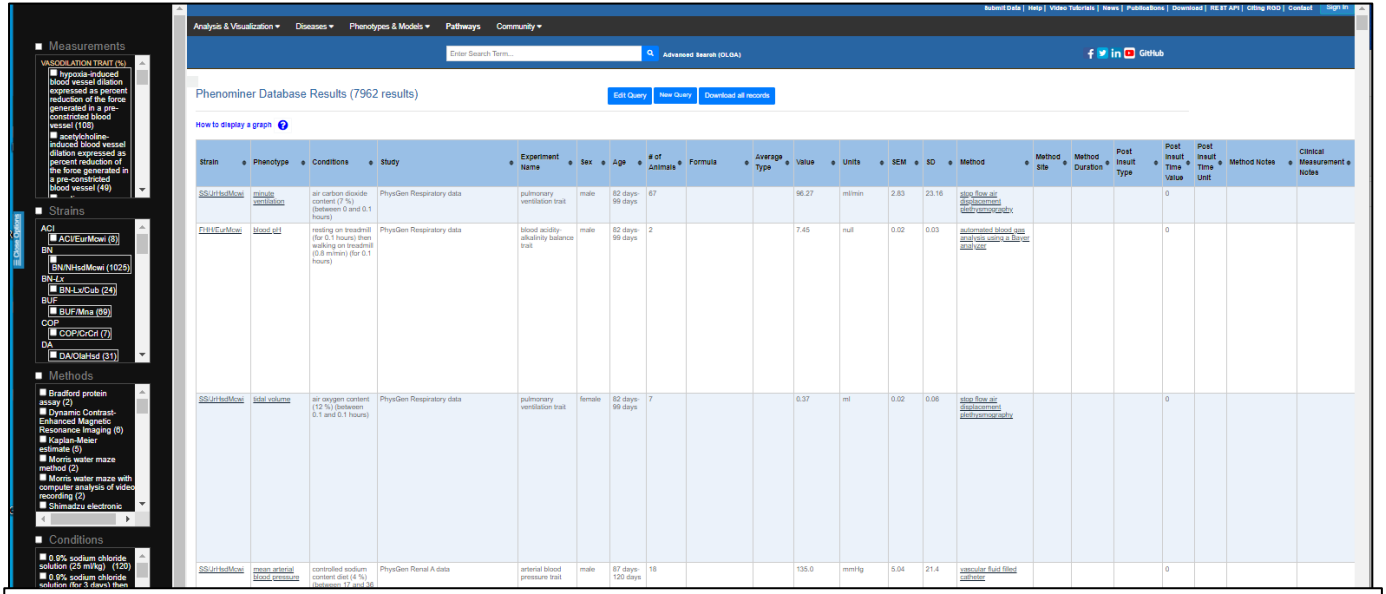

PhenoMiner will open with available strains preselected, and all available phenotype data for those strains shown in a downloadable report table. A graph cannot display phenotypes with varying units of measure, so left-side filters are available to make selections.

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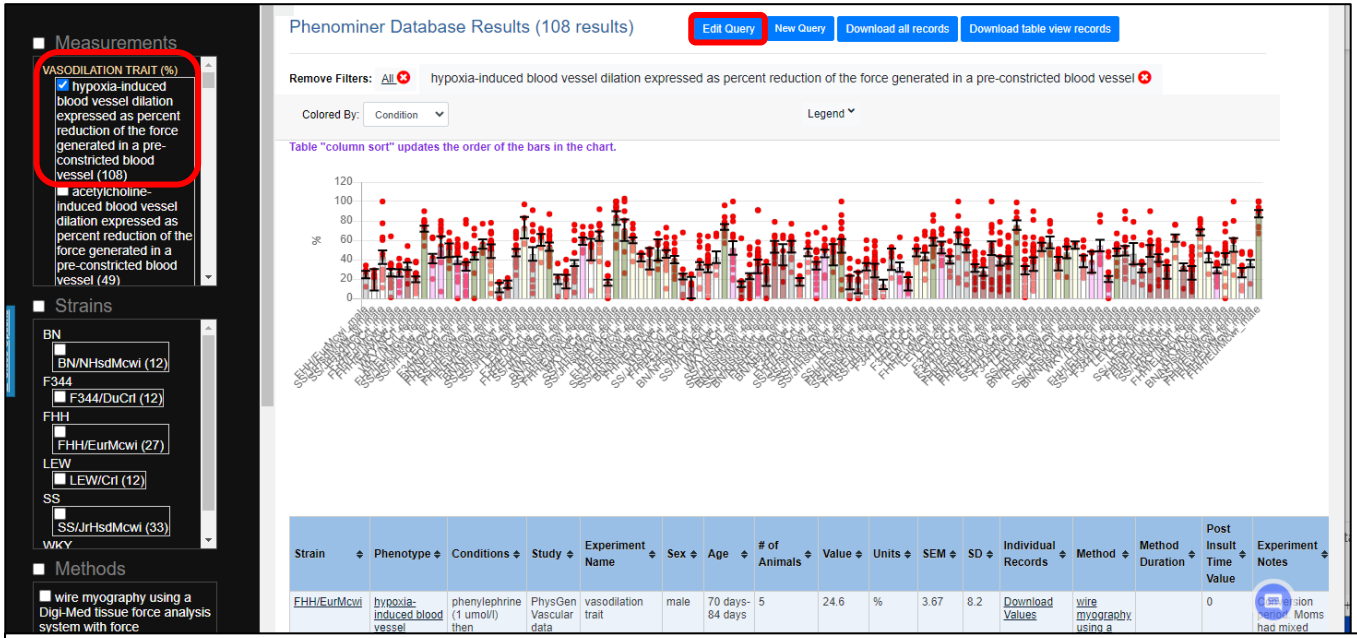

For example, selecting the very first trait available in the list limits the data to a single % unit of measure, and now the graph can display. Alternatively one could select Edit Query to open the data selection page.

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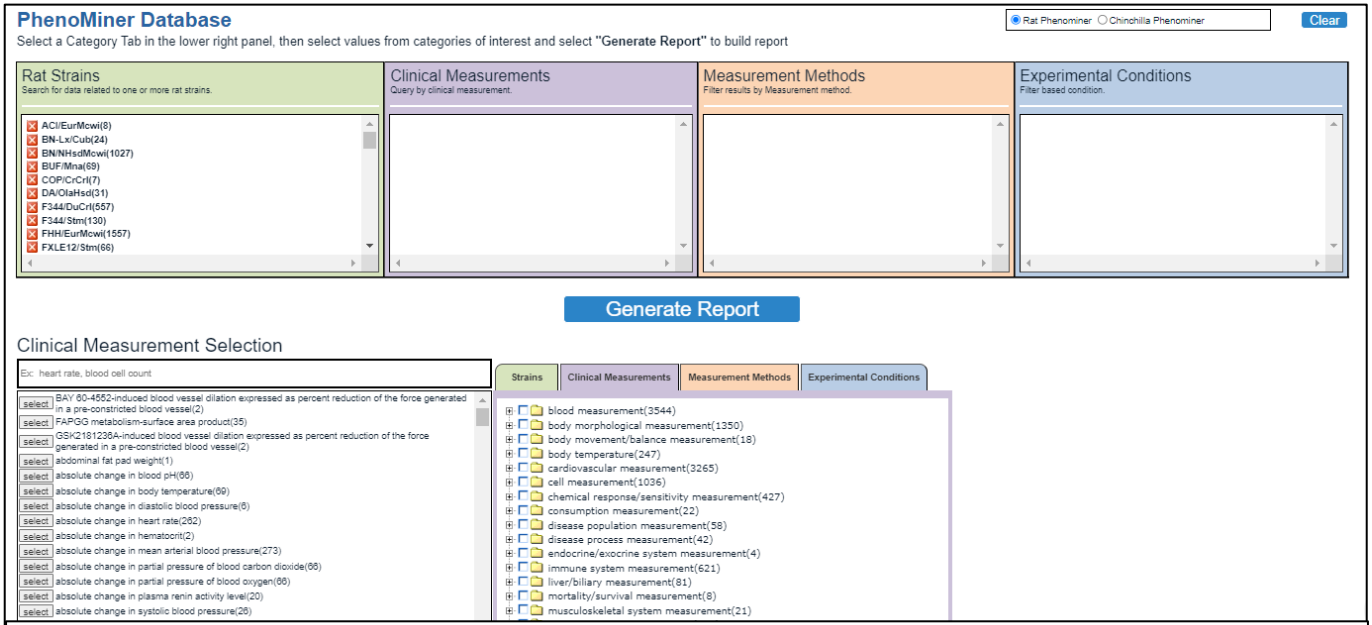

Edit Query will open the user interface for data selection and allow options for tailoring the list of strains, clinical measurements or other parameters. The Generate Report button will return the user to the data interface page with the table.

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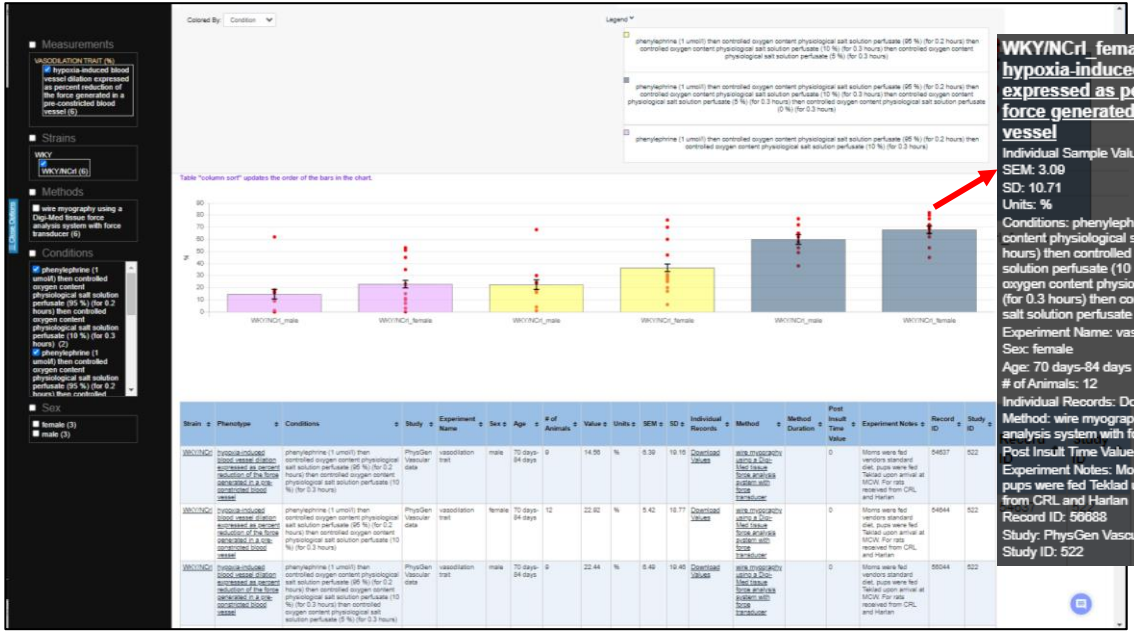

WKY/NCrl_female
hypoxia-induced blood vessel dilation expressed as percent reduction of the force generated in a pre-constricted blood vessel
Individual Sample Value - 4: 77
SEM: 3.09
SD: 10.71
Units: %
Conditions: phenylephrine (1 umol/l) then controlled oxygen content physiological salt solution perfusate (95 %) (for 0.2 hours) then controlled oxygen content physiological salt solution perfusate (10 %) (for 0.3 hours) then controlled oxygen content physiological salt solution perfusate (5 %) (for 0.3 hours) then controlled oxygen content physiological salt solution perfusate (0 %) (for 0.3 hours)
Experiment Name: vasodilation trait
Sex: female
Age: 70 days-84 days
# of Animals: 12
Individual Records: Download Values
Method: wire myography using a Digi-Med tissue force analysis system with force transducer
Post Insult Time Value: 0
Experiment Notes: Moms were fed vendors standard diet, pups were fed Teklad upon arrival at MCW. For rats received from CRL and Harlan
Record ID: 56688
Study: PhysGen Vascular data
Study ID: 522

Strain	Phenotype	Conditions	Study	Experiment Name	Sex	Age	# of Animals	Value	Units	SEM	SD	Individual Records	Method	Method Duration	Post Insult Time Value	Experiment Notes	Record ID	Study ID
WKY/NCrl	hypoxia-induced blood vessel dilation expressed as percent reduction of the force generated in a pre-constricted blood vessel	phenylephrine (1 umol/l) then controlled oxygen content physiological salt solution perfusate (95 %) (for 0.2 hours) then controlled oxygen content physiological salt solution perfusate (10 %) (for 0.3 hours) then controlled oxygen content physiological salt solution perfusate (5 %) (for 0.3 hours)	PhysGen Vascular data	vasodilation trait	male	70 days-84 days	9	14.56	%	6.39	19.16	Download Values	wire myography using a Digi-Med tissue force analysis system with force transducer		0	Moms were fed vendors standard diet, pups were fed Teklad upon arrival at MCW. For rats received from CRL and Harlan	54637	522
WKY/NCrl	hypoxia-induced blood vessel dilation expressed as percent reduction of the force generated in a pre-constricted blood vessel	phenylephrine (1 umol/l) then controlled oxygen content physiological salt solution perfusate (95 %) (for 0.2 hours) then controlled oxygen content physiological salt solution perfusate (10 %) (for 0.3 hours) then controlled oxygen content physiological salt solution perfusate (5 %) (for 0.3 hours)	PhysGen Vascular data	vasodilation trait	female	70 days-84 days	12	22.92	%	5.42	18.77	Download Values	wire myography using a Digi-Med tissue force analysis system with force transducer		0	Moms were fed vendors standard diet, pups were fed Teklad upon arrival at MCW. For rats received from CRL and Harlan	54644	522
WKY/NCrl	hypoxia-induced blood vessel dilation expressed as percent reduction of the force generated in a pre-constricted blood vessel	phenylephrine (1 umol/l) then controlled oxygen content physiological salt solution perfusate (95 %) (for 0.2 hours) then controlled oxygen content physiological salt solution perfusate (10 %) (for 0.3 hours) then controlled oxygen content physiological salt solution perfusate (5 %) (for 0.3 hours)	PhysGen Vascular data	vasodilation trait	male	70 days-84 days	9	22.44	%	6.49	19.46	Download Values	wire myography using a Digi-Med tissue force analysis system with force transducer		0	Moms were fed vendors standard diet, pups were fed Teklad upon arrival at MCW. For rats received from CRL and Harlan	56044	522

On the graph display, composite data is shown as the bars and individual rat data is shown as red datapoints. Both data types are downloadable. Hovering over a bar or individual datapoint will display all the parameters for that data value.

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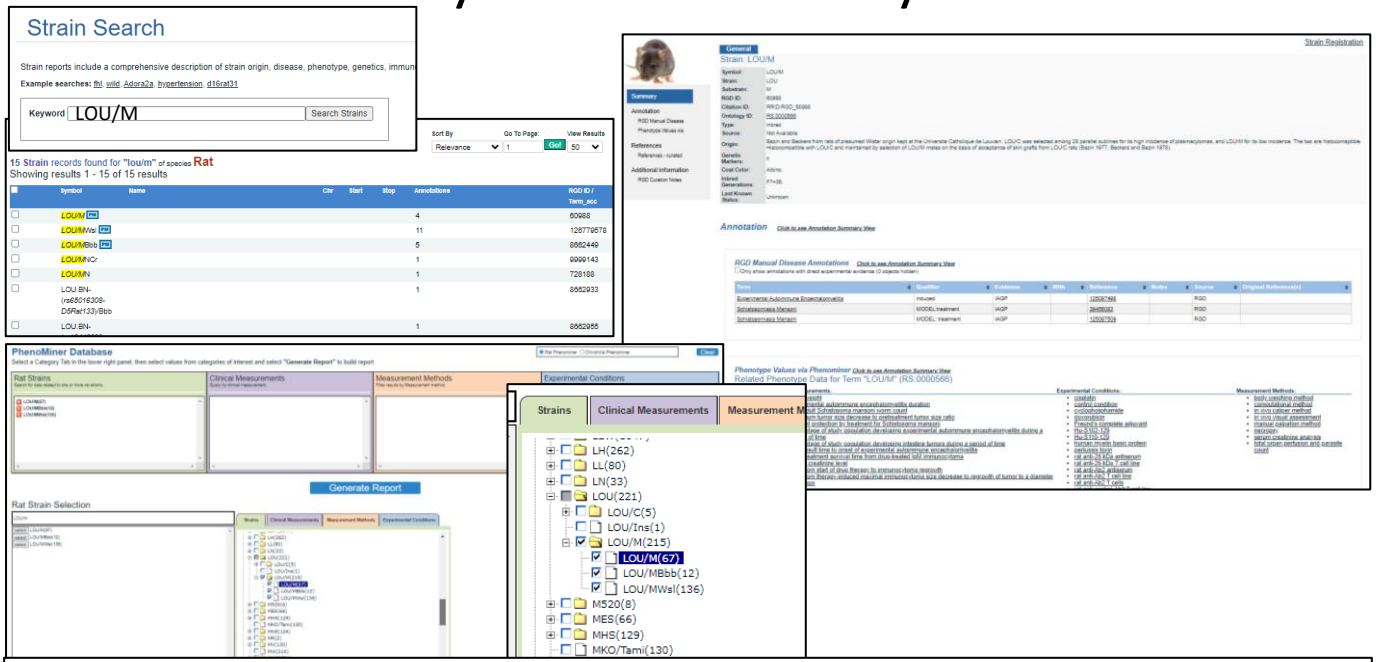

To revisit briefly the issue of closely related strains and substrains;
In some cases very little data was found for the HRDP original strain. More data is available adding closely related or derived substrains.

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The Hybrid Rat Diversity Panel

- Has a wealth of data available at RGD.
- The HRDP portal page under Phenotypes and Models holds the lists of strains with links to strain report pages and tools.
- Strain report pages have curated and imported data.
- Variant Visualizer is loaded with the sequencing data for an increasing number of HRDP strains.
- PhenoMiner has data curated from literature, and uploaded from investigators, for a number of the HRDP strains, particularly the inbred strains.

Acknowledgments

Rat Genome Database

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