Cre Portal (<u>www.creportal.org</u>) Tutorial

<u>This tutorial contains two parts</u>: first, a step-by-step example that you can use to follow along on your computer; and second, a short set of questions (with answers) for you to test your skills.

Aims

- 1. Find your way to the Cre Portal and search for a cre transgene or knock-in that uses a particular driver/promoter or is known to have activity in a particular anatomical/tissue system.
- 2. Explore the contents of the Results Page returned and learn about customizing it for your use.
- 3. Explore detailed information about the cre activity of a specific cre transgene or knock-in and learn about customizing the view and linking to other data.
 - Cre construct information
 - · Availability of mouse resources from repositories
 - Specifics of cre activity/specificity for a transgene in an anatomical location (here reproductive system)
 - Images
 - Publications involving this cre transgene/knock-in
 - Phenotypes observed when mice carrying this cre transgene/knock-in were mated to different gene knock-out heterozygotes
- 4. Return to the Cre Portal main page and view the data report for 'all cre transgenes/knock-ins'.

Introduction

Cre is currently the most commonly used recombinase. It catalyzes site-specific recombination of DNA between loxP sites, thus making possible conditional mutagenesis, where specific genes can be knocked-out in particular tissues and at particular developmental time points. Other non-cre recombinases (such as Flp, Dre, phiC31, etc.) and various inducible forms of recombinases have been and are being developed. The Cre Portal contains curated data about all recombinase containing transgenes and knock-ins developed in mice to provide a comprehensive resource delineating known activity patterns and allowing users to find relevant mouse resources for their studies.

At present, researchers can search for "cre" data using the driver/promoter gene symbol or using an anatomical system in which the "cre" is expressed. In addition, data are available for all cre's in a HTML viewable table, or as downloadable tab-delimited text.

Help with using the Cre Portal is available on the <u>www.creportal.org</u> site. See the list of FAQs in the right-hand column or the 'Help Documents' tab in the bottom section of this page. You can also use the 'Contact Us' link in the navy blue navigation bar near the top of any of our web pages.

Worked examples:

 Find the Cre Portal and search for a cre transgene or knock-in with a particular driver/promoter [or with cre activity in a particular anatomical/tissue system]. Type the URL: <u>http://www.creportal.org</u> into your web browser; OR go to the Mouse Genome Informatics (MGI) homepage (<u>http://www.informatics.jax.org</u>) and select the Recombinase (cre) icon. The following illustrates the latter route: visiting the MGI homepage and selecting the icon.





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2. Explore the contents of the Results Page returned from your search and learn about customizing it for your use.

This is the default Results Page from the search illustrated on the previous page. Now let's explore the features of this page.

Recombinase Alleles - Tissue Summary

You sea Driver equ	arched f uals Pbsn	for:		<<	first < prev 1 n	iext > last >>	25 🗘)
Click colu	mn headin	gs to sort table data.				Showing item	is 1 - 8 of 8	
Driver 🌲	Matrix View	Allele Symbol Gene; Allele Name	Recombinase Activity Detected	Recombinase Activity Not Detected	Induced By $\hat{\Rightarrow}$	Find Mice (IMSR)	Refs 🔺	Allele Synonym
Pbsn		Tg(Pbsn-cre)4Prb transgene insertion 4, Pradip Roy-Burman	renal & urinary system, reproductive system	alimentary system, cardiovascular system, embryo-other, head, hemolymphoid system, integumental system, liver & biliary system, nervous system, respiratory system		2	247	ARR2PB-Cre, PB-Cre4, PB-Cre, PbCre4
Pbsn		hypoxanthine guanine phosphoribosyl transferase; targeted mutation 1, Frank R Jirik			tamoxifen		2	ARR2PB-CreER(T2)
Pbsn		Pbsnem1(cre/ERT2)Smoc probasin; endonuclease-mediated mutation 1, Shanghai Model Organisms Center			tamoxifen		1	Pbsnem1(V5-2A-CreERT2-WPRE- polyA)Smoc
Pbsn		Pbsnem1(icre)Gpt probasin; endonuclease-mediated mutation 1, GemPharmatech Co., Ltd					1	Pbsn-iCre
Pbsn		Tg(ARR2/Pbsn-icre)58Atai transgene insertion 58, Atsu Aiba	renal & urinary system, reproductive system	cardiovascular system, liver & biliary system, respiratory system			1	PB-iCre58
Pbsn		Tg(Pbsn-cre)4Prb transgene insertion 4, Pradip Roy-Burman	renal & urinary system, reproductive system	alimentary system, cardiovascular system, embryo-other, head, hemolymphoid system, integumental system, liver & biliary system, nervous system, respiratory system		2	247	ARR2PB-Cre, PB-Cre4, PB-Cre, PbCre4
Pbsn		Tg(Pbsn-cre)20Fwan transgene insertion 20, Fen Wang	renal & urinary system, reproductive system	mouse-other		1	27	ARR2PB-Cre, ARR2PBi-Cre, PRR2Bi-Cre, Tg(Pbsn-Cre)
Pbsn		Tg(Pbsn-cre)8113ANg transgene insertion 8113A, Norman M Greenberg					6	PB-Cre [8113-A], PB-Cre
Pbsn		Tg(Pbsn-cre/Esr1*)14Abch transgene insertion 14, Andreas Birbach			tamoxifen	2	2	ProbasinBAC-MerCreMer

The columns of the table can be sorted (as indicated by the up/down arrows in the column headers) and reordered (by placing the cursor in any column header). For example, perhaps you want an alphabetic sort of the Drivers in your Results Page; or to sort by the number of references (an indicator of how widely this cre line is used); or to sort by the Find Mice column to bring all those cre lines that are in public repositories to the top of your Results Page.

Driver -

View

Matrix Allele Symbol Gene: Allele Name Recombinase Activity Detected

Each line of the table provides basic information about the cre transgene or knock-in. Within a row of data, each of which represents a single cre line transgene or knock-in, there are a number of links and actions possible that lead to further data details (shown below).

The link in the Allele Symbol column directs you to a page showing phenotypes reported in offspring of mice bearing this cre transgene and mice carrying floxed alleles of various genes (see page 11 of this tutorial).

If there are recombinase activity data for any allele using a driver that is a mouse gene, a grid icon will appear in the Matrix View column for all alleles that use that mouse driver gene. The icon links to a matrix which allows you to compare endogenous wild-type gene expression with reported recombinase activity data.

The **Recombinase Activity Detected** and **Not Detected** columns show the anatomical systems where cre activity has been "Detected in..." or "Not detected in..." In turn, each anatomical system term is a link directing you to a page showing the data for cre activity in that system (next page of this tutorial).

The number displayed in the **Find Mice (IMSR) column** is a link to the International Mouse Strain Resource (IMSR) page with information on what repository holds relevant cre lines and how to obtain them.

The number in the **Refs column** shows the number of publications about this cre and links to the full list of these publications (this number gives an idea of how widely this particular cre transgene has been used experimentally).

Driver 🤤	Matrix View	Allele Symbol Gene; Allele Name	Recombinase Activity Detected	Recombinase Activity Not Detected	Induced By 🍦	Find Mice (IMSR)	Refs 🔺	Allele Synonym
Pbsn		Tg(Pbsn-cre)4Prb transgene insertion 4, Pradip Roy-Burman	renal & urinary system, reproductive system	alimentary system, cardiovascular system, embryo-other, head, hemolymphoid system, integumental system, liver & biliary system, nervous system, respiratory system		2	247	ARR2PB-Cre, PB-Cre4, PB-Cre, PbCre4

Step 3. Click on the allele symbol for **Tg(Pbsn-cre)4Prb** to go to the allele detail page to find cre activity/specificity in the reproductive system for this cre transgene.

3. Explore detailed information about the cre activity of a specific cre transgene or knock-in and learn about customizing the view.

On the Tg(Pbsn-cre)4Prb Transgene Detail page (shown on page 9), in the Recombinase activity section, click on one of the colored cells for reproductive system. In the pop-up that launches, click on View All Result Details and Images.

Below is the cre specificity detail page for **Tg(Pnsn-cre)4Prb in the Reproductive System**. Many rows of the **Recombinase Activity** table have been omitted to save space in this tutorial document. We will explore each sections of this page (delineated by the blue title column at left).

?			Tg(Pbs	sn-cre)4	Prb - Reprodu	active tail	e Systen	n			
			Allele Infor	mation Tiss	ue Information Image	s Reco	mbinase Activ	vity References			
Allele Information	Allel	e: Tg(Pbsn-c transgene ins	ertion 4, Pradig	Roy-Burman	Driver: Pbsn Type: Transgenic (Cr	e/Flp)				(A)	
	Synonyn	n: PB-Cre4, PB-C	cre, PbCre4, AF	R2PB-Cre							
	Molecular description	The transgene expression in t very low level	is composed of the prostatic ep of transgene e	f the cre recomplication of the cre recomplication of the technication of technica	binase gene under the cont transgene is expressed post detected in the seminal ves	rol of a co natally in icles, test	prosite promot prostatic epithel es, and ovaries.	ter derived from rat Pi ium with the highest I No transgeneexpressi	osn. The rat evel of exp on was det	Pbsn promoter dr ression in the late ected in any of the	rives postnata ral lobe of the other tissue
	Find mice (IMSR): Mouse Strain	ns: 1 lines av	vailable C	ell Lines: 0 lines availat	le					
Tissue Information	Reproductive System	Other recombin	ase alleles w	hith activity in ^{13(cre)Bhr} , Cal	Reproductive System	tissues: cre)Zjh	.(more)			В	
Images	Drag images to compare to	o others or to data	in the table be	elow. Drag corn	ers to resize images for mo	re detail.	Reset Images	8			
	J:68167 Fig. 2	:68167 Fig. 3	J:68167	Fig. 4	J:68167 Fig. 5						
-											
Recombinase	Click heading to re-sort tal	ble.	< prev	1 next>	50 \$						
			Showi	ng items 1 - 32	2 of 32		Assays	Genotypic Back	ground	Result Notes	s
	Structure -	Assayed Age	Level 🌲	Pattern 🌲	Reference, Source 🌲	Assay	Туре	Reporter Gene	Detectio	on Method	Assay Note
	ductus deferens	postnatal week 8	Ambiguous	Not Specified	J:68167 Fig. 2A	Recombi	nase reporter	lacZ	direct		
	ductus deferens	postnatal week 2	Ambiguous	Not Specified	J:68167 Fig. 5D	Recombi	nase reporter	lacZ	direct		
	epididymis	postnatal week	Absent	Not	J:68167	Recombi	nase reporter	lac7	direct		

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testis	postnatal week 8	Present	Spotted		Recombinase reporter	lacZ	direct
testis	postnatal week 8	Present	Not Specified	J:68167 No figure available	Recombinase reporter	lacZ	direct
uterus	postnatal week 8	Absent	Not Applicable	J:68167 No figure available	Recombinase reporter	lacZ	direct

References All for this allele: 76 reference(s)

A. Allele Information. This section contains essentials about the cre transgene itself; its correct <u>nomenclature</u> (symbol and name), the <u>driver</u> involved, other <u>synonyms</u> that have been used in publications, a <u>molecular</u> <u>description</u> of the what the transgene is carrying (in this case, the cre recombinase gene under the control of a composite promoter derived from the rat *Pbsn* gene) and a '<u>Find mice</u>' IMSR summary indicating whether mice or cell lines carrying this transgene are available from public repositories.

B. Tissue Information. This section lists all other cre transgenes and knock-ins that have reported activity in the Reproductive System. Each symbol is a link to the cre specificity page for that transgene or knock-in for the Reproductive System. The ...(more) indicates there are others and clicking on (more) will bring back the entire list.

?			Tg(P	bsn-cre)	4Prb - Repro	ductive Syst	em		
			Allele Ir	formation Ti	ssue Information Im	ages Recombinase A	Activity References		
Allele Information	Alle	le: Tg(Pbsn-c	ertion 4, Pr	adip Roy-Burmar	Driver: Pbsn	(Cre/Flp)			
	Synonyi	m: PB-Cre4, PB-C	Cre, PbCre4	, ARR2PB-Cre					
	Molecular descriptio	The transgene expression in	is compose the prostati	ed of the cre reco c epithelium. The	mbinase gene under the transgene is expressed is detected in the seminal	control of a composite pro costnatally in prostatic epi	omoter derived from rat P thelium with the highest	bsn. The rat Pbsn promoter level of expression in the la	r drives postnata ateral lobe of th
	Find mice (IMSR	R): Mouse Strai	ns: 1 line	s available	Cell Lines: 0 lines ava	ilable	nest no cransgeneexpress	ion has acceled in any or	
Tissue Information	Reproductive System	Other recombin	nase allele ^{agy} , Amhr	s with activity 2 ^{tm3(cre)Bhr} , C	in Reproductive Syste alb2 ^{tm1(cre)Zjh} , Cck tm	em tissues: 1.1(cre)Zjh(more)			
Images	Drag images to compare t	to others or to data	in the tabl	e below. Drag co	mers to resize images for	more detail. Reset Ima	ges		
Recombinase	2:68167 Fig. 2	3:68167 Fig. 3):68	167 Fig. 4	2:68167 Fig. 5	Assays	Genotypic Back	ground Result No	tes
	Structure -	Assayed Age	Level	Pattern	Reference, Source	Assay Type	Reporter Gene	Detection Method	Assay Not
	ductus deferens	postnatal week 8	Ambiguou	Not Specified	J:68167 Fig. 2A	Recombinase reporte	er lacZ	direct	
	ductus deferens	postnatal week 2	Ambiguou	Not Specified	J:68167 Fig. 5D	Recombinase reporte	er lacZ	direct	D
	epididvmis	postnatal week	Absent	Not	J:68167	Recombinase reporte	er lacZ	direct	
					//				
	testis	postnatal 8	week	Present	Spotted		Recombinase repor	ter lacZ	direct
	testis	postnatal 8	week	Present	Not J:68 Specified No	167 figure available	Recombinase repor	ter lacZ	direct
	uterus	postnatal 8	week	Absent	Not J:68 Applicable No	167 figure available	Recombinase repor	ter lacZ	direct
References	All for this allele:	76 reference	e(s)					(E)	

C. Images. This section presents a gallery of thumbnail images for cre activity for the tissue being viewed. Images can be enlarged by dragging at the corners and may be moved around the window for convenient viewing. Enlarging an image also activates a pop-up with caption and attribution information.

D. Recombinase Activity. This tabular section provides the annotation detail for the cre activity, including anatomical structure, age, activity level & pattern, and data source. The last columns of the table (separated by a gray bar) are controlled by tabs at the top of the table and allow this section of the table to show variably 'Assay' or 'Genotypic Background' information or 'Result Notes'. The view shown here is 'Assay' information, consisting of Assay Type, Reporter Gene, Detection Method, and Assay Notes. Observe that all columns in this table are sortable, as indicated by the up/down arrowheads after the column heading title. For example, one might want to sort by age to group all data together for a certain age; or by structure; or by level to place all the 'present' vs. 'absent' together. Finally, clicking on the sm all image in the table highlights the corresponding image in the image gallery so it is easier to identify the image you may want to enlarge.

E. References. This section lists the number of publications for this cre transgene and links to the full list.

Now we will look at some of the links and actions on this page....

?			Tg(Pbs	sn-cre)4 _{R€}	Prb - Repro	Detail	e Syster	n		
			Allele Infor	mation Tis	sue Information Ir	nages Reco	mbinase Acti	vity References		
Allele Information	Alle Synony Molecular descripti Find mice (IMS	Tg(Pbsn-c transgene ins Ym: PB-Cre4, PB-C The transgene The transgene on: expression in very low level R): Mouse Strain	tre)4Prb ertion 4, Pradij Cre, PbCre4, AF is composed of the prostatic ep of transgene e ns: 1 lines ar	o Roy-Burman RR2PB-Cre of the cre recon bithelium. The expression was vailable	Driver: Pbsn Type: Transgeni nbinase gene under the transgene is expressed detected in the semina Cell Lines: 0 lines av	C (Step Find D Infor Sum	1 . Clicl <u>Mice (II</u> mation. mary p	c on the '1 lii <u>MSR</u>) section This brings age (below)	ne available' i n of the Allele you to the IM	n the SR
Tissue Information	Reproductive System	M Other recombin ► Alpl ^{tm1(cre)N}	ase alleles v ^{agy} , Amhr2 th	with activity in ^{n3(cre)Bhr} , Ca	n Reproductive Syst Ib2 ^{tm1(cre)Zjh} , Cck ^{tr}	en assocs. n1.1(cre)Zjh	.(more)			
Images	J:68167 Fig. 2	Dice others or to data):68167	Fig. 4	Step 2. C section to ins known Clicking o compara	lick on t see all to expr n any of ble Rec	he 'more of the o ress in the f the syr ombina	e' in the <u>Tiss</u> ther cre tran he Reproduc nbols will bri ise Activity	sue Informations sgenes and k ctive System. ing you to the Detail page .	in nock- ir
Recombinase Activity	Click heading to re-sort t	able. 🜖	< prev Showi	1 next > ng items 1 - 32	50 ÷ 2 of 32		Assays	Genotypic Backg	round Result No	otes
	Structure -	Assayed Age	Level 🌲	Pattern 🤤	Reference, Source	Assay	Туре	Reporter Gene	Detection Method	Assay Not
	ductus deferens	postnatal week 8	Ambiguous	Not Specified	J:68167 Fig. 2A	Step 3.	Enlarge	an image b	y dragging at	its
	ductus deferens	postnatal week 2	Ambiguous	Not Specified	J:68167 Fig. 5D	corners	and mo	ve to a conv	enient viewing	g ga 8)
	epididymis	postnatal week	Absent	Not	J:68167					

Below, Result of Step 1. View of IMSR (International Mouse Strain Resource) results and access to a Tg(Pbsn-cre)4Prb bearing strain.

6			Interna	tional Mou	se Strain R	esource (IM	ISR)	
	J Se	earch Repo	sitories	Participate	Glossary	Contact Us	About Us	
Expo	rt: 📄 🗵		Filter by:	State 7 Type 7 Pr	ovider 7 Mutation 7			
Ν	Strain Name	Synonyms	States	Repository 🗘	Mutation Types	Alleles		Genes
-	B6.Cg- Tg(Pbsn- cre)4Prb? &	B6.D2-Tg(Pbsn- cre)4Prb,B6;D2- Tg(Pbsn- cre)4Prb,PB- Cre4,B6.Cg- Tg(Pbsn- cre)4Prb	live		recombinase(cre/flp)	Tg(Pbsn-cre)4Prb transgene insertio	값 n 4, Pradip Roy-Burman	Tg(Pbsn-cre)4Prb & transgene insertion 4, Pradip
							\mathbf{i}	

Links to repository's strain information page

Repository abbreviation and email link for questions or to order mice. (NCIMR is the NCI Mutant Resource) Link to MGI allele/phenotype page for this transgene (later in this tutorial, page 9) **Below, Result of Step 2**. List of all other cre transgenes and knock-ins that show activity in the Reproductive Systerm (there are 100 listed here). Each symbol is a link to the respective Reproductive System cre details for that transgene or knock-in. Note the (less) at the end of the list, which will collapse the list back to its original few.

Tissue	Other recombinase alleles with activity in Reproductive System tissues:
Information	W Alpfm1(cre)May Anhr2m3(cre)Bir Calb2 ^{m1} (cre)2 ^j , Cctim1.1(cre)2 ^j , Cdtm1.1(cre)2 ^j , Chat ^{m1} (cre)2 ^j , Crt ^{m1} (cr

Below, Result of Step 3. The enlarged image was made by dragging the image corners. If you click an image, the image legend and attribution pops up to the right of the image. Multiple images may be enlarged and moved as you work. Note the 'Reset Images' Button (arrow) that can be used to bring all images enlarged or moved back to their original size and placement on this page.



Finally, we learn about <u>phenotypes observed</u> when mice carrying a particular cre transgene/knock-in are mated to mice carrying different genes with loxP sites (genes that will be knocked-out when exposed to cre recombinase).

enoty By clic arch su	pe data ca king on the ummary pa	an be acce e <u>phenotyp</u> age (see p	e ssed e i <u>e data</u> li age 5 o	i ther : ink in the f the tutor	cre ial).		OR	2. By <u>kno</u>	clicki <u>ock-in</u>	ng c <u>syn</u> De	on the <u>t</u> nbol or tail pag	ransgen i the Re ge (start	i <u>e or</u> combina ing at pa	ase age {
Driver equals	Pbsn eadings to sort table data	Drag headings to rearrand	e columns.						X	01.0		nai)		
Dahara	Allele Symbol	¢	Recombinase		Nervous	Reprod	uctive 🚊	Find Mice						
Pbsn	 Gene, Allele Name Hprt^{tm1}(Pbsn*-cre/ hypoxanthine guanine transferase; targeted mutation 1 l (phenotype data) 	RT2)Jir 2 phosphoribosyl Frank R Jirik	No data availab	le	System	System		2	_					
Pbsn	Tg(Pbsn-cre)20Fv transgenic insertion 2	van 0, Fen Wang	 Detected in 1 sy Not detected in 1 	stem. 2 systems.		Detect	ed	6						
Phsn	Tg(Pbsn-cre)4Pt	Pradio Rov-Burman	?			Allelen	Tg(Pbs	-cre)4Prb - Recombinase Sp ssue Information Images	eproduc becificity Deta	il e Specificity	ystem			
10311	(phenotype data)	, Hadip Koy-barman	e ir Allele S Information	Alle	le: Tg(Pbsn-c	cre)4Prb	p Roy-Burman	Driver: Pbsn	e/Fin)					
Pbsn	Tg(Pbsn-cre)8113 transgene insertion 8 Greenberg (phenotype data)	ANg 113A, Norman M	S	Synony Molecular descriptio	m: ARR2PB-Cre, The transgene in the prostat transgene ex;	PB-Cre, PB-Cre e is composed o ic epithelium. T pression was de ins: 1 lines a	4, PbCre4 of the cre recor he transgene i tected in the s	binase gene under the cont expressed postnatally in pre- eminal vesicles, testes, and of Cell Lines: 0 lines availa	rol of a composit ostatic epitheliu ovaries. No trans	te promoter m with the h sgeneexpress	derived from rat Pbs ighest level of expre- sion was detected in	n. The rat Pbsn promote ssion in the lateral lobe o any of the other tissue t	r drives postnatal trans of the prostate gland. A ypes examined.	igene expressi Very low leve
			Tissue Information	Reproductive Syste	M Other recom	binase allele	s with activit	y in Reproductive Syste	m tissues: m1(cre)Lowl(n	nore)				
			Images	Drag images to compare to Figals(7) 19.2 19.2 19.2 19.3 19.3 19.3 19.3 19.3 19.3 19.3 19.3 19.3 19.3 19.3 19.3 19.3 19.5	p others or to data 77 Picture Pictur	in the table bel	(ow. Drag com D:68167 Fig. 5	rs to resize images for more	e detail. <mark>Reset 1</mark>	tmages				
			Recombinase Specificity	Click heading to resort tal	ole. 🕄				Assays	Genotyp	oic Background	Result Notes		
				Structure	Assayed Age postnatal week 2	Level 💲 Ambiguous	Pattern 🗘 Not Specified	Reference, Source 🗘 J:68167 Fig. SD	Assay Type Recombinase	ç	Reporter Gene 😓	Detection Method Direct Detection	Assay Note	
				ductus deferens	postnatal week 8	Ambiguous	Not Specified	J:68167 Fig. 2A	Recombinase	reporter	lacZ	Direct Detection		

This is the **Transgene detail page for Tg(Pbsn-cre)4Prb, which contains the phenotype data**. Like the Recombinase Activity page for the Reproductive System, the information at the top of the page is basic information on nomenclature, the description of the molecular construct and includes links to IMSR to obtain mice carrying this transgene. There is also a section summarizing recombinase activity with links to the Recombinase Activity pages as we have reviewed previously. Two phenotype sections on this page, labeled

?					Т	g(Pb	sn-c	re)	4Prb)												[Your	Input	Weld	ome
-	Nomenc	lature	Transgene origin Tra	nsgene d	escriptio	n Expr	ansgene [ession F	Detail Recon	nbinase	activi	ty P	henot	ypes	Di	sease m	nodels	Fir	nd Mi	ce (IMS	R)	Refere	ences				
Nomenclature	Symbo Nam MGI I Synonym Transger	ol: T ne: tr ID: M ns: Al ne: T <u>c</u>	g(Pbsn-cre)4Prb ansgene insertion 4, P GI:2385927 RR2PB-Cre, PB-Cre, Pb g(Pbsn-cre)4Prb Locat	radip Ro OCre4, Pf <i>ion:</i> unk	y-Burm 3-Cre4 nown	an							,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,				Prost grad neop Brca cre) ² Sho ima allel	tate h e pros lasia 2 ^{tm1B} IPrb/(w the ge(s) e.	yperplas state intr in "/Brca2) mice) mice e 9 phe) involv	sia an raepit tm1Br enoty	d low- helial ⁿ Tg(Pb /pe this	isn-				
Transgene	Strain of (Origin	: (C57BL/6 x DBA/2)F	1																			Lars -	N. IF		
Transgene description	Transgeno Mu	e Type Itation	 Transgenic (Reco Insertion Mutation details: drives postnatal tran lateral lobe of the pu in any of the other t 	mbinase The trans isgene exp rostate gla issue type	e) sgene is o pression ind. A ve is examir	composed in the pro ry low lev hed. (<i>J:68</i>	d of the cre ostatic epit vel of trans 3167)	e reco heliur sgene	mbinase n. The tr expressi	gene ansge on wa	under ne is e s dete	the co express ected in	ontrol o sed po the s	of a ostna semir	composi atally in I nal vesic	te pron prostat les, tes	note ic ep stes,	r deriv itheliu and o	ved from um with ovaries. I	n rat F the h No tra	Pbsn. T ighest ansgen	he rat l level of e expre	Pbsn pr f expres ssion w	omoter sion in ras dete	the	
Recombinase activity	Activity:	Act	tivity in Systems/Structu how or hide all structures Legend nentary system diovascular system bryo-other nolymphoid system ad gumental system wous system al & urinary system roductive system piratory system	Impose Impose <td< th=""><th>Bysonice fermi errit</th><th>3.8.91 Erv C C C C C C C C C C C C C C C C C C C</th><th>2,339 profice [EA profice [EA Howe Howe 1 0 1 1 0 1 1 0 1 0 1 1 1 1 1 1 1 1 1 1 1 1 1</th><th>21) orn (Pr 0 0 0 0 0</th><th>39 2 2 3 4 4 4 4 4 4 4 4</th><th></th><th>.9) Adult</th><th>0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0</th><th></th><th>11898</th><th>urspecifi</th><th>eed)</th><th></th><th></th><th></th><th></th><th></th><th></th><th></th><th></th><th></th><th></th></td<>	Bysonice fermi errit	3.8 .91 Erv C C C C C C C C C C C C C C C C C C C	2,339 profice [EA profice [EA Howe Howe 1 0 1 1 0 1 1 0 1 0 1 1 1 1 1 1 1 1 1 1 1 1 1	21) orn (Pr 0 0 0 0 0	3 9 2 2 3 4 4 4 4 4 4 4 4		.9) Adult	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0		11898	urspecifi	eed)										
	Driver:	Pb	osn (rat) Summary of all re	combinas	e alleles	driven by	Pbsn.	Com	parative	matrix	view	of rec	ombin	nase	activities	5										
Phenotypes	ŀ	Key:	hm homozygous	ht hete	erozygou	s	faat in t	tg in	volves t	ansge	nes	datas	in etc		√ phen	otype o	obse	rved								_
	Genot	ype/	ch conditional genotype	Allelic	Compos	sition	e reature	UL OL	ner: ner	mzygo	us, inc	uetern	intate,	Ger	netic Ba	iai priel	ound	Je						Cell L	.ine(s)	
	Backgrou	und:	cn1	Eaf1 ^{tm1} . Tg(Pbsn	1Zhow/Ea	f1 ^{tm1.1Zh} b/0	ow							B6(Cg)-Eaf1	tm1.1Zh	how T	g(Pbs	n-cre)4l	Prb						0
	В)	cn2	Pten ^{tm11} Cop1 ^{tm2} Tg(Pbsn	Hwu/Pten 1Vmd/Co -cre)4Prt	tm1Hwu pp1 ^{tm2.1V} p/0	md							B6N	I.CgCop1	tm2.1Vr	^{md} Pt	en ^{tm1}	^{LHwu} Tg(Pbsn-	cre)4Pi	rb				
			cn3	Tg(Pbsn	-cre)4Prt	p1 ⁺ p/0 p1tm2.1V	md							B6N	I.CgCop1	tm2.1V	md Pt	en ^{tm1}	LHWU Tg(Pbsn-	cre)4Pi	rb				
	Phenoty	pes:	Affected Systems show or hide all annotated terr	ns			Sex: of	l cn	2 cn3	<u>cn4</u> ଫ	<mark>ന5</mark> റ്	<mark>cn6</mark> ර	cn7	cn d	8 cn9	<mark>cn10</mark> 오 ơ	f c	11 5	cn12 c	n13	cn14	cn15		<mark>cn17</mark> ර්	<mark>ന18</mark> ്	<mark>сп19</mark> ♀ с
			endocrine/exocrine	glands			• •		· •	~	~	✓	~		/ 1	v	/ ,	/					v v √	√	√	

(A) Phenotypes and (B) Genotypes are described below.

Affected Systems show or hide all annotated terms cellular endocrine/exocrine glands homeostasis/metabolism immune system mortality/aging renal/urinary system reproductive system tumorigenesis reproductive system reproductive system phe	en1 en2 en3 en4 en4 Sex: o o o o o Image:	5 ♂ ✓	A. The high-le affecte conjur genot 'Affect Genot along unique there to mon table f	e Phenot evel look ed in mice nction wit ype). This ted syste type (row the top o e genotyp is a toggl re detaile from the l ne toggle	types Section provides a at the kinds of systems e carrying this transgene in h other genes (the s section displays a matrix of ms' (left column) by), where each abbreviation f the matrix represents a be. As in other examples, e (▶) that expands the table d data. <u>Left</u> , a copy of the Phenotype Page (page 10) circled. <u>Below</u> , the
abnormal bulbourethral	gland morphology		expan	ision of th	rie reproductive system terms
abnormal prostate gland	morphology		aunou		nous genolypes.
enlarged prostate gla	nd anterior lobe				
abnormal prostate gla	and branching morphogen	esis			
abnormal prostate gla	and epithelium morpholog	v			
prostate gland en	ithelial hyperplasia	·			
decreased prostate of	and weight				
enlarged prostate gla	nd				
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abnormal prostate gland	prysiology		Y I		
prostate giand inflam	mation				
female infertility				V	
Rfwd2 ^{tm2.1Vmd} /Rfwd2 ^{tm2.1Vmd}	d Key: phenotype observed in females f phenotype observed in mal	WTSI Wellcome In	Trust Sanger stitute phenome		
B6N.Cg-Rfwd2 Tg(Pb cre)4Prb	N normal phenotype	Luit			

reproductive system

prostate gland hyperplasia (J:172653)

- O^{*} in 3 of 4 mice at 40 weeks of age (J:172653)
- in all mice at 52 weeks of age (J:172653)

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abnormal prostate gland physiology ( J:172653 )
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O* • cells in the ventral and lateral prostate exhibit increased proliferation compared to in wild-type mice (J:172653)

normal phenotype

tumorigenesis

prostate intraepithelial neoplasia (J:172653) ${\ensuremath{\textup{O}}}^{\bullet}$ \bullet low grade in 2 of 6 mice at 52 weeks of age (J:172653)

endocrine/exocrine glands

- prostate gland hyperplasia (J:172653)
 - O^{*} in 3 of 4 mice at 40 weeks of age (J:172653) • in all mice at 52 weeks of age (J:172653)

abnormal prostate gland physiology (J:172653)

 σ • cells in the ventral and lateral prostate exhibit increased proliferation compared to in wild-type mice (J:172653)

B. Genotypes. Each genotype includes its allelic composition and genetic background. The third conditional genotype described, cn3, includes the Tg(Pbsn-cre)4Prb transgene and Rfwd2 targeted alleles on a congenic B6N background. Click on the cn3 button to open a new window containing phenotypic details reported in the mice (shown at left).

4. Return to the Cre Portal main page & view the data report for 'all cre transgenes/knock-ins'

Find the Cre Portal main page using http://www.creportal.org. Locate the "Retrieve All Alleles Section" and choose either the MGI Recombinase Alleles Report (an html page view format) or the Tab-delimited version if you wish to copy the file into Excel or some other analysis program.

0					(?) Keywords, Symbols, or IDs	Quick Search
Help	FAQ	ome Genes Phenotypes Expre	ession Recomb	inases Function	Pathways Strains / SNPs Ho	mology Tumors
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GI collec	Re cts and annotates expressio	combinase (cre) Act	Livity containing transge	nes and knock-in a	illeles.	8
Access	Data			FAQs		
FIND REC Search f Search f	Tor alleles assayed for specific recombinase activity in the second seco	city/activity in an anatomical structu in: r activity. y: (choose one) + Go	ire.	More FAQs Cre Portal Tutorial	existing recombinase-expressing tra -ins that have a given promoter (driv the promoter (driver) that I'm lookin e selection list? FAQ a recombinase-containing transgenes e expressed in a specific tissue? FAQ a full list of all transgenes and knock ss recombinase? FAQ er mice with a desired recombinase c	Insgenes and ver)? FAQ Ing for if it is not e or knock-in t-ins that construct? FAQ
Retriev	e a list of all recombinase-co MGI Recombinase Alleles Rej Tab-delimited version	ontaining transgenes and knock-in al	leles.	560 Rei 1,383 Rei 1,943 Tot 544 Dri Step 1 Step 2 of the h	. Locate the file link of . Follow the link. Here the bage version of the link of . Follow the link. Here	f interest. a few lines are shown.
FI Rec report pro allele syn national N arch for fl arch repor	ombinase Alleles Rep vides a list of all recombinase-con nbol is linked to its respective MG fouse Strain Resource (IMSR) stra loxed, frt, or other recombinase tar sitories for specific strains carrying	ort taining alleles in the MGI database. I Allele Detail page, containing phenotypic ar in if a repository holds mice carrying the liste get-containing alleles in MGI, use the <u>Phenot</u> g mutations of all types, use the <u>IMSR Search</u>	nd disease model data; ed allele. <u>type and Alleles Query</u> <u>Form</u> .	each Anatomical Syste	m for an allele is linked to its MGI Recombir	nase Detail page. A link is provid
ver	Allele Symbol	Name	Detected in	Absent in	IMSR Strain	A
408G22Rik 0038C07Rik	8430408G22Rik ^{tm1(EGFP/crc)Shin} Tg(A930038C07Rik-crc)4Aibs Tg(AAT-crc)31Rbrc	RIKEN cDNA 8430408G22 gene; targeted mutation 1, Donghun Shin transgene insertion 4, Ed Lein transgene insertion 31, RIKEN BioResource Center			B6:C3-Tg(A930038C07Rik-cre)4Aibs/J C57BL/6J-Tg(AAT-cre)31Rbrc/Rbrc	M
	Tg(AAT-cre)43Rbrc	transgene insertion 43, RIKEN BioResource Center			C57BL/6J-Tg(AAT-cre)43Rbrc/Rbrc	М
a	12g(AAI-cre)50Rbrc Te(Abpa-cre)1Cmal	transgene insertion 1, Charles M Allan	reproductive system		C5/BL/6J-Tg(AAI-cre)50Rbrc/Rbrc	M
n	Acan ^{tm1(cro/ERT2)Crm}	aggrecan; targeted mutation 1, Benoit de Crombrugghe	embryo-other limbs postnatal-other respiratory system sensory organs	cardiovascular system liver & biliary system nervous system renal & urinary system		M
5	Tg(Acp5-cre)4Rda	transgene insertion 4, Rachel A Davey	alimentary system cardiovascular system head liver & biliary system postnatal-other respiratory system			М
5	Tg(Acp5-cre)3Rda	transgene insertion 3, Rachel A Davey	alimentary system head hemolymphoid system liver & biliary system postnatal-other			M

Self Directed Tasks

1. Using the Cre Portal, find cre carrying transgenes or knock-ins that are driven by *AMH*. How many are there?

Which one do you think has been used most experimentally?

Are any mice available with these cre transgenes from public repositories? If so, from where? For the *AMH* driven cre transgenes, what tissues are listed as "not detected" for cre recombinase activity? What ages were assayed?

(explanation note: You will note that the search is case in-sensitive. In your results you will see AMH and Amh cre alleles. This is because nomenclature follows that of the species where the gene originated. AMH is the human gene (all capital letters); Amh is the mouse gene (first letter only capitalized).

2. For Plekha5^{Tg(AMH-cre)1Flor}, what tissues were reported with staining 'Present' (indicating cre activity) at postnatal day 35?

What reporter gene was used in the assays for Plekha5^{Tg(AMH-cre)1Flor} and Tg(Amh-cre)8815Reb?

3. For Plekha5^{Tg(AMH-cre)1Flor}, when mated to other targeted mutations, what other classes of phenotypes are observed in addition to "reproductive" related?

Answers (These are likely to change due to database updates, etc.)

1. From <u>www.creportal.org</u>, select the driver *Amh* in the 'search for alleles by promoter/driver specificity' and then click 'GO'.

There are 6 cre transgenes with an *Amh* driver. Two are driven by the human *AMH* promoter, the other 4 by the mouse *Amh* promoter. These symbols follow species' nomenclature convention. You can also learn this by reading the molecular description in the transgene detail pages.

Because there are 107 references for Plekha5^{Tg(AMH-cre)1Flor}, this allele is likely to have been used most frequently.

Yes, 2 of these cre transgenes are available from public repositories. Plekha5^{Tg(AMH-cre)1Flor} is available from the EMMA repository (EM) in Europe as frozen embryos. Tg(Amh-cre)8815Reb is available from the Jackson Laboratory repository (JAX) as sperm.

On the summary page, for the Plekha5^{Tg(AMH-cre)1Flor} transgene, in the Recombinase Activity Not Detected column, the data indicate recombinase (cre) activity is not detected in the anatomical class "embryo-other". Following this link to this 'anatomical class' one sees that cre activity was not detected at embryonic day 12.5 and 13.5.

2. For Plekha5^{Tg(AMH-cre)1Flor} at day 35, staining was found in ovary antral follicle, ovary secondary follicle and ovary stratum granulosum.

The reporter gene for cre transgene Plekha5^{Tg(AMH-cre)1Flor} was lacZ; for cre transgene Tg(Amh-cre)8815Reb, the reporter gene was hemagglutinin.

3. Through the "phenotype data" link for Plekha5^{Tg(AMH-cre)1Flor}, you can see that there are cellular, endocrine/exocrine gland, homeostasis/metabolism, and immune system phenotypes observed.

We welcome your feedback in improving this resource. Contact us through the "Contact Us" link in the navy blue navigation bar at the far right; or email <u>mgi-help@jax.org</u>