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				<<	first < prev 1 n	ext > last >>	25 🗘)
Click colur	nn headin	gs to sort table data.				Showing item	s 1 - 8 of 8	
Driver \diamondsuit	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
Pbsn		hypoxanthine guanine phosphoribosyl transferase; targeted mutation 1, Frank R Jirik			tamoxifen		2	ARR2PB-CreER(T2)
bsn		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
bsn		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
bsn		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)
bsn		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		Prb - Reprodu		e Syster	n		
			Allele Infor	mation Tis	sue Information Image	s Reco	mbinase Acti	vity References	-	
Allele Information	Alle	le: Tg(Pbsn-c transgene inse		o Roy-Burman	Driver: Pbsn Type: Transgenic (Cr	e/Flp)			A	
	Synony	m: PB-Cre4, PB-C	re, PbCre4, AF	RR2PB-Cre						r
	Molecular descriptio	n: expression in t	he prostatic e	oithelium. The	nbinase gene under the cont transgene is expressed post detected in the seminal ves	natally in	prostatic epithe	lium with the highest l	evel of expression in the la	ateral lobe of the
	Find mice (IMSF	R): Mouse Strain	ns: 1 lines a	vailable C	Cell Lines: 0 lines availab	le				
Tissue Information	Reproductive System	Other recombin Alpl ^{tm1(cre)Na}	ase alleles w ^{Igy} , Amhr2 th	vith activity in ^{n3(cre)Bhr} , Ca	n Reproductive System Ib2 ^{tm1(cre)Zjh} , Cck ^{tm1.1}	tissues: cre)Zjh	.(more)		В	
Images	Drag images to compare t	o others or to data	in the table be	elow. Drag corr	ners to resize images for mo	re detail.	Reset Image	s		
	0:68167 Fig. 2	J:68167 Fig. 3):68167	Fig. 4	D:68167 Fig. 5					
Recombinase Activity	Click heading to re-sort ta	able.		1 next > ng items 1 - 32	50 ‡ 2 of 32		Assays	Genotypic Back	ground Result No	tes
	Structure -	Assayed Age	Level 🌲	Pattern 🗘	Reference, Source 🌲	Assay	Туре	Reporter Gene	Detection 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.

			Allele Info	ormation Tis	sue Information Imag	ges Recombinase A	ctivity References		
Allele Information	Allel	transgene ins		dip Roy-Burman	Driver: Pbsn Type: Transgenic (C	Cre/Flp)			
	Synonyr	n: PB-Cre4, PB-C	cre, PbCre4, A	ARR2PB-Cre					
	Molecular descriptio	n: expression in	the prostatic	epithelium. The	mbinase gene under the con transgene is expressed pos detected in the seminal ve	stnatally in prostatic epi	thelium with the highest	level of expression in the	lateral lobe of t
	Find mice (IMSR	-	-		Cell Lines: 0 lines availa				
Tissue Information	Reproductive System	Other recombin	ase alleles ^{agy} , Amhr2 ¹	with activity i tm3(cre)Bhr, Ca	in Reproductive System alb2 ^{tm1(cre)Zjh} , Cck ^{tm1.}	tissues: ^{1(cre)Zjh} (more)			
Images	Drag images to compare to	o others or to data	in the table	below. Drag cor	mers to resize images for m	nore detail. Reset Ima	ges		
	J:68167 Fig. 2	J:68167 Fig. 3	J:6816	57 Fig. 4	J:68167 Fig. 5				
								С	
lecombinase Activity	Click heading to re-sort ta	ble. 1	<pre>c prev Show</pre>	1 next > wing items 1 - 3	50 ÷ 2 of 32	Assays	Genotypic Back	ground Result N	otes
	Click heading to re-sort ta	ble. 1 Assayed Age\$		wing items 1 - 3	2 of 32 Reference, Source		Genotypic Back Reporter Gene		
	Structure -		Show	ving items 1 - 3	2 of 32		Reporter Gene		
	Structure	Assayed Age postnatal week	Show	Ving items 1 - 3	2 of 32 Reference, Source J:68167 Fig. 2A	Assay Type	Reporter Gene	Detection Method	
	Structure ductus deferens ductus deferens	Assayed Age postnatal week 8 postnatal week	Show	Ving items 1 - 3	2 of 32 Reference, Source (3:68167 Fig. 2A):68167 Fig. 5D):68167 J:68167	Assay Type Recombinase reporte	Reporter Gene ar lacZ ar lacZ	Detection Method	
Recombinase Activity	Structure ductus deferens ductus deferens	Assayed Age postnatal week postnatal week postnatal week postnatal week	Show Level Ambiguous Ambiguous Absent	Ving items 1 - 3	2 of 32 Reference, Source 3:68167 Fig. 2A 3:68167 Fig. 5D 3:68167 J:68167	Assay Type Recombinase reporte Recombinase reporte	Reporter Gene er lacZ er lacZ	Detection Method direct direct	Assay Not
	Structure	Assayed Age postnatal week 8 postnatal week 2 postnatal week	Show Level Ambiguous Ambiguous Absent	ving items 1 - 3 Pattern Pattern Not Specified Not Specified Not Not	2 of 32 Reference, Source (3:68167 Fig. 2A):68167 Fig. 5D):68167 J:68167	Assay Type Recombinase reporte Recombinase reporte	Reporter Gene ar lacZ ar lacZ	Detection Method direct direct	
	Structure	Assayed Age postnatal week postnatal week postnatal week postnatal week	Show Level Ambiguous Ambiguous Absent week P	ving items 1 - 3 Pattern Pattern Not Specified Not Specified Not Not	2 of 32 Reference, Source J:68167 Fig. 2A J:68167 Fig. 5D J:68167 // Spotted Not Spotted J:6816 J:6816	Assay Type Recombinase reporte Recombinase reporte Recombinase reporte Recombinase reporte	Reporter Gene er lacZ er lacZ	Detection Method direct direct rter lacZ	Assay Not

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		Prb - Repr		e Syste	m								
			Allele Infor	mation Tiss	sue Information	Images Reco	mbinase Act	ivity References								
Allele Information	Alle	le: Tg(Pbsn-c transgene inst	re)4Prb ertion 4, Pradip	Roy-Burman	Driver: Pbsn Type: Transger	nic (Step	1. Clic	k on the '1 lir	ne available' i	n the						
	Synony	m: PB-Cre4, PB-C	re, PbCre4, AR	R2PB-Cre		Find	Find Mice (IMSR) section of the Allele									
	Molecular descriptio	n: expression in t	he prostatic ep	ithelium. The t	binase gene under th ransgene is expresse detected in the semi-		Information. This brings you to the IMSR									
	Find mice (IMSR	t): Mouse Strain	ns: 1 lines av	vailable C	ell Lines: 0 lines a	wail Sum	mary p	age (below)								
Tissue Information	Reproductive System	Other recombin Alpl ^{tm1(cre)Na}	ase alleles w	ith activity in ^{13(cre)Bhr} , Cal	h Reproductive Sy Ib2 ^{tm1(cre)Zjh} , Cck	tm1.1(cre)Zjh	.(more)									
Images	Drag images to compare t	o others or to data	in the table be	low. Drag corn	ers to resize images	for more detail.	Rese Image	es								
	J:68167 Fig. 2	J:68167 Fig. 3	J:68167	Fig. 4	J:68167 Fig. 5											
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			. 🥗													
Recombinase Activity	Click heading to re-sort ta	able. 1		1 next > ng items 1 - 32	50 ÷ 2 of 32		Assays	Genotypic Backg	round Result No	tes						
	Click heading to re-sort ta	Assayed Age¢			Reference, Source	ce Assay		Genotypic Backg Reporter Gene	round Result No							
	-		Showin	ng items 1 - 32			Туре	Reporter Gene	Detection Method	Assay N						
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Below, Result of Step 1. View of IMSR (International Mouse Strain Resource) results and access to a Tg(Pbsn-cre)4Prb bearing strain.

- Ig(PDSn- Cre)APrD,PB- cre)4Prb? ₪ Cre4,B6.Cg- Tg(Pbsn- Tg(Pbsn-			MSR)	esource (II	ise Strain R	tional Mou	Internat	I		5
N Strain Name ○ Synonyms States Repository ○ Mutation Types Alleles Genes - B6.Cg- Tg(Pbsn- cre)4Prb,B6;D2- Tg(Pbsn- cre)4Prb,PB- cre)4Prb,PB- cre)4Prb,PB- cre(4,B6.Cg- Tg(Pbsn- cre)4Prb? @ Ive NCIMR NCIMR recombinase(cre/fip) Tg(Pbsn-cre)4Prb @ Tg(Pbsn- transgene insection 4, Pradip Roy-Burman Tg(Pbsn- transgene insection 4, Pradip Roy-Burman			About Us	Contact Us	Glossary	Participate	sitories	arch Repos	Sea	
- B6.Cg- Tg(Pbsn- cre)4Prb,PB- cre)4Prb? ☆ Cre4,B6.Cg- Tg(Pbsn- cre)4Prb? ☆ Tg(Pbsn- cre)4Prb? \end{pmatrix} Tg(Pbsn- cre)4Pr					ovider 7 Mutation 7	State 7 Type 7 Pr	Filter by:		rt: 📒 🗵	Expo
- B6.Cg- Tg(Pbsn- cre)4Prb,B6;D2- Tg(Pbsn- cre)4Prb,PB- Cre4,B6.Cg- Tg(Pbsn- cre)4Prb? Tg(Pbsn- cre)4Prb? Tg(Pbsn- Cre4,B6.Cg- Cre4,B6.Cg- Tg(Pbsn- Cre4,B6.Cg- C		Genes		Alleles	Mutation Types	Repository 🔅	States	Synonyms	Strain Name 🗘	Ν
cre)4Prb	n-cre)4Prb & gene insertion 4, Prad	Tg(Pbsn-cre)4 -Burman transgene ins			recombinase(cre/flp)		live	cre)4Prb,B6;D2- Tg(Pbsn- cre)4Prb,PB- Cre4,B6.Cg-	Tg(Pbsn-	-

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 Information

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).

By clic arch su	king on the ummary pa	an be acce e <u>phenotyp</u> age (see p	<u>e data</u> li	ink in the			OR	,		De	<u>nbol</u> or	ransgen h the Re ge (start rial)	combina	
Driver equals Click column he		Drag headings to rearrang	ge columns.						X	01.0		iidi)		
Driver	Allele Symbol Gene; Allele Name	\$	Recombinase Data	;	Nervous System	Reprod System	uctive 😄	Find Mice						
Pbsn	hypoxanthine guaning transferase;	RT2)Jir e phosphoribosyl Frank R Jirik	No data availab	le				2						
Pbsn	Tg(Pbsn-cre)20Fw transgenic insertion 2 (phenotype data)		 Detected in 1 sy Not detected in 1 			Detect	red	6						
Pbsn	Tg(Pbsn-cre)4P transgene insertion 4	Pradio Bou Rurman	,?			Allela	/	n-cre)4Prb - Recombinase Sp ssue Information Images	ecificity Deta	il	-			
PUSIT	(phenotype data)	, Flaup Roy-burnan	e ir Allele ^S Information	Alle	le: Tg(Pbsn-			Driver: Pbsn Type: Transgenic (Cri						
Pbsn	Tg(Pbsn-cre)8113 transgene insertion 8 Greenberg (phenotype data)		N		m: ARR2PB-Cre, The transgen in the prostat transgene exp	PB-Cre, PB-Cre e is composed o ic epithelium. T pression was de	4, PbCre4 of the cre recor he transgene i stected in the s	binase gene under the cont expressed postnatally in pre eminal vesicles, testes, and o Cell Lines: 0 lines availa	ostatic epithelius ovaries. No trans	m with the h	ighest level of expre	ssion in the lateral lobe of	of the prostate gland. A	
			Tissue Information	Reproductive Syste	Other recom	binase allele	s with activit	y in Reproductive Syste		nore)				
			Images	Drag images to compare the second sec			low. Drag corn D:68167 Fig. 5	rs to resize images for more	e detail. Reset 1	Images				
			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	¢	Reporter Gene 😓	Detection Method Direct Detection	Assay Note	;
				ductus deferens	postnatal week 8	Ambiguous	Not Specified	J:68167 Fig. 2A	Recombinase	reporter	iacZ	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		sn-ci		Prb)												٦	Your	Input	Welc	ome
	Nomeno	lature	Transgene origin Tra	nsaene d	escriptio		ansgene E ression R		binase	activi	tv I P	henot	vpes	I Di	isease n	nodels	1 Fir	nd Mi	ce (IMS	R) I I	Refere	nces				
Nomenclature	Symb Nan MGI Synonyn	ne: tr ID: M ns: A	g(Pbsn-cre)4Prb ansgene insertion 4, P GI:2385927 RR2PB-Cre, PB-Cre, Pt g(Pbsn-cre)4Prb <i>Local</i>	Pradip Ro DCre4, PE	y-Burm 3-Cre4						-,		,,,				Pros grad neop Brca cre)4 Sho	tate h e pros lasia i 2 ^{tm1Bi} iPrb/0 w the	yperplas state intr	ia and raepiti tm1Brr	d low- helial ¹ Tg(Pb: pe	*				
Transgene	Otacia of	O ut at last															alle	e.					SP)			
origin	Strain or	Ungin	: (C57BL/6 x DBA/2)F	-1																						
Transgene description	managen	e Type utatior		: The trans nsgene exp rostate gla	sgene is o pression ind. A ve	in the pro ry low lev	static epiti el of trans	helium	. The tr	ansge	ne is e	expres	sed po	ostna	atally in	prostat	ic ep	itheliu	um with t	the hi	ighest l	evel of	expres	sion in	the cted	
Recombinase activity	Activity:	Act	tivity in Systems/Structo how or hide all structures Legend	ures	anyonic (En	08.91 Ent	orgonic Eth	211 por	3.9) weating	3 (PA-2	.9) Ining (P242.	stnatal	11/296	unspecifi	ledi										
		alin	nentary system	<u>ب</u> ور الم		 	~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~ ~	୍ ୧୯	୧ ୦	0-	PO.	°	7													
		car	diovascular system	• •	0	0	0	0	0			0														
		em	bryo-other	• •																						
		hea	d	• •	0	0	0	0	0			0														
		her	nolymphoid system	•	0	0	0	0	0			0														
		inte	egumental system	•	0	0	0	0	0			0														
		live	er & biliary system	•	0	0	0	0	0			0														
		ner	vous system	• •	0	0	0	0	0			0														
		ren	al & urinary system	•	0	0	0		0			0														
		rep	roductive system	•	0	0			0			0														
		res	piratory system	•	0	0	0	0	0			0														
	Driver:		osn (rat) Summary of all room		e alleles	driven by	Pbsn.	Comp	arative	matrix	view	of rec	ombin	nase	activities	S										
Phenotypes		Key:	hm homozygous		erozygou			tg inv	olves tr	ansge	nes				√ phen											
	Genot	ype/	cn conditional genotype		oplex: >	-	e feature	ot otr	er: her	nizygo	us, in	determ			N norm									Coll I	.ine(s)	
	Backgro		cn1	Eaf1 ^{tm1.}		f1 ^{tm1.1Zh}	ow								Cg)-Eaf1	-			n-cre)4P	rb				Cell L	.ine(s)	
	В)	cn2	Pten ^{tm11} Cop1 ^{tm2} Tg(Pbsn	Hwu/Pten 1.1Vmd/Co -cre)4Prt	tm1Hwu pp1 ^{tm2.1Vi} p/0	md							B6N	N.CgCop:	1 ^{tm2.1V}	md Pl	en ^{tm1}	^{LHWU} Tg(F	Pbsn-	cre)4Pr	ъ				
			cn3	Tg(Pbsn	-cre)4Prt	p1 ⁺ p/0 p1tm2.1V	nd							B6N	N.CgCop:	1 ^{tm2.1V}	md Pl	en ^{tm1}	^{LHwu} Tg(F	Pbsn-	cre)4Pr	ъ				
	Phenoty	pes:	Affected Systems show or hide all annotated ten				Sex: 0		<mark>cn3</mark> ර්	<mark>cn4</mark> ଫ	cn5 ්	<mark>cn6</mark> ර	cn7	C	n8 cn9 ර ර	<mark>cn10</mark> 우 C			cn12 cr	n13	cn14	cn15	<mark>cn16</mark> ♀ ♂	cn17 0	<mark>cn18</mark> ර්	cn19 Q (
			cellular																				√ √			
			endocrine/exocrine	glands			▶ √	√	✓	✓	✓	✓	√	1	< √	l l	/	/					V	✓	√	ا

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

Affected Systems show or hide all annotated terms	en1 en2 en3 en4 en5 Sex: ♂ ♂ ♂ ♀ ♂		The Phenotypes Section provides a
cellular			gh-level look at the kinds of systems fected in mice carrying this transgene ir
endocrine/exocrine glands			injunction with other genes (the
homeostasis/metabolism			enotype). This section displays a matrix
immune system			ffected systems' (left column) by
mortality/aging			enotype (row), where each abbreviation
renal/urinary system reproductive system			ong the top of the matrix represents a nique genotype. As in other examples,
tumorigenesis			ere is a toggle () that expands the tak
			more detailed data. Left, a copy of the
reproductive system	+		ble from the Phenotype Page (page 10)
reproductive system photo-	enotype		th the toggle circled. <u>Below,</u> the pansion of the reproductive system terr
abnormal bulbourethral	gland morphology		tributed to various genotypes.
abnormal prostate gland	i morphology		
enlarged prostate gla	and anterior lobe		
abnormal prostate g	land branching morphogenesis	5	
abnormal prostate g	land epithelium morphology		
prostate gland ep	oithelial hyperplasia		
decreased prostate g	land weight		
enlarged prostate gla	and		
increased prostat	e gland weight		
prostate gland hy	/perplasia	✓	· · ·
abnormal prostate gland	j physiology	✓	
prostate gland inflam	nmation		
female infertility			✓
Rfwd2 ^{tm2.1Vmd} /Rfwd2 ^{tm2.1Vm}	phenotype observed in females W	TSI Wellcome Trust Sange Institute	nger
B6N.Cg-Rfwd2 ^{tm2.1Vmd} Tg(P cre)4Prb	bsn- N normal phenotype	Ph Europhenome	

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)

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	lome Genes Phenotypes Expre	ession Recomb	inases Function	Pathways Strains / SNPs Ho	mology Tumors
ch 🔻			ind Mice (IMSR			
GI colle		combinase (cre) Act		nes and knock-in a	alleles.	8
Access	Data			FAQs		
Search f	for alleles assayed for specific recombinase activity for alleles by promoter/drive recombinase active by promoter/drive recombinase driven by the r	Go r activity.	ire.	knock find on the find that is get expre	existing recombinase-expressing tra -ins that have a given promoter (driv the promoter (driver) that I'm looking a selection list? FAQ a recombinase-containing transgenes expressed in a specific tissue? FAQ a full list of all transgenes and knock as recombinase? FAQ er mice with a desired recombinase of	ver)? FAQ ng for if it is not e or knock-in -ins that
Bernye	VE ALL ALLELES				Allele Data Include	12 Jun 2013
Iev	MGI Recombinase Alleles Re Tab-delimited version	ontaining transgenes and knock-in al		1,383 Ret 1,943 Tot 544 Dri Step 1 Step 2	combinase-containing knock-in alleles combinase-containing transgenes al recombinase transgenes and alleles vers in recombinase transgenes . Locate the file link of . Follow the link. Here timl web page version	a few lines
report pro allele syn national N arch for fi	nbol is linked to its respective MG Mouse Strain Resource (IMSR) stra loxed, frt, or other recombinase tar	ort ttaining alleles in the MGI database. If Allele Detail page, containing phenotypic and in if a repository holds mice carrying the lister rget-containing alleles in MGI, use the <u>Phenot</u> g mutations of all types, use the <u>IMSR Search</u>	ed allele. type and Alleles Query		m for an allele is linked to its MGI Recombir	aase Detail page. A link is provid
ver	Allele Symbol	Name	Detected in	Absent in	IMSR Strain	A
0038C07Rik	8430408G22Rik tm1(EGFP/cre)Shin Tg(A930038C07Rik-cre)4Aibs Tg(AA7-cre)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 C57BL/6J-Tg(AAT-cre)31Rbrc/Rbrc	M M M
	Tg(AAT-cre)43Rbrc Tg(AAT-cre)50Rbrc	transgene insertion 43, RIKEN BioResource Center transgene insertion 50, RIKEN BioResource Center			C57BL/6J-Tg(AAT-cre)43Rbrc/Rbrc C57BL/6J-Tg(AAT-cre)50Rbrc/Rbrc	M
a	Tg(Abpa-cre)1Cmal	transgene insertion 50, RIKEN BioResource Center transgene insertion 1, Charles M Allan	reproductive system		CST DL/OJ-1 g(AA1-CTC)30KDTC/KDTC	M
1	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		pr
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>